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COMPOUND FRACTURES

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A compound fracture is a broken bone with an associated wound of the overlying skin. Even if the wound does not actually communicate with the fracture line, the intervening tissue barrier may be insufficient to prevent spread of infection.

PATHOLOGIC PICTURE

It makes little difference whether the wound of the skin is caused by protrusion of the bone fragment from within or by the force from without. The tissue is potentially infected in either case. The prognosis and thoroughness of treatment are influenced greatly by the conditions under which the wound was received. The prevalence of the more severe pathogenic organisms is greater in manured fields, horse-inhabited streets and stables, shell-torn country and dirty clothes than it is in the woods, in steel mills or in clean houses. Uninjured, clean clothing and careful protection in transportation are comforting incidents. The severity and extent of the damage to the soft parts are important factors. The element which determines success or failure most of all is the interval which elapses between the original injury and the institution of proper treatment. Every quarter-hour counts in getting rid of the invading organism and devitalized tissue.

TREATMENT

General Principles.—The objects of treatment are threefold: (*a*) to care for the general condition of the patient; (*b*) to obtain healing of the broken bone with the best possible alinement of the fragments and the least possible impairment of function, and (*c*) to prevent or control infection.

(*a*) Patients with compound fractures often have multiple injuries and show varying degrees of shock. Treatment of the latter should be instituted immediately, but only with pulseless, moribund patients should treatment of shock be allowed to delay operative procedures beyond the time required for obtaining necessary roentgen evidence and preparation

of the operating room. Treatment of shock is continued in the operating room while other surgical measures are being carried out.

(*b*) The principles of treatment of the bone are the same for compound as for closed fractures:

1. Minimize the secondary trauma of transportation and examination.
2. Reduce displacements early and accurately.
3. Immobilize sufficiently the broken bone.
4. Mobilize early the adjacent joints and muscles.
5. Maintain local circulation at its optimum.

(*c*) The principles of prevention or control of infection are as follows:

1. Protect the wound and immobilize the injured part before transportation.
2. At the earliest possible moment, surgically remove all foreign material and devitalized tissue.
3. Avoid tension in the wound.
4. Provide rest for the injured part.
5. Administer serums and drugs to combat organisms.

Details of Treatment.—1. Shock: If the injured part has not been splinted properly before the patient arrives at the hospital, this should be done before he is moved from the transporting vehicle. Morphine should be given immediately to reduce pain and lessen muscular spasm. Rest and heat may be all that is necessary while roentgen and other examinations are made, but if the pulse, pressure and hematocrit readings indicate it saline solution, dextrose or blood should be given first. Unless the symptoms of shock are marked, administration of these substances can be carried out during the operative procedures. The best way to lessen shock is to get the débridement and immobilization done as soon as possible.

2. Chemotherapy: Antitetanic serum should always be given. If gas-forming organisms are suspected, prophylactic serums may be included. The use of sulfanilamide and the related drugs as a routine procedure is still debatable. In some clinics sulfanilamide is now used either locally or generally. In view of the complications and sequelae our plan is to use it only when smears or cultures after débridement yield bacteria.

3. Débridement: This term has been universally adopted to describe operative removal from a wound of contaminating foreign material and devitalized tissue. The success of the procedure will depend on the time at which it is done and on the thoroughness and gentleness with which it is carried out. If it is done within a few hours of the accident one may hope to remove most of the contaminating material. After

twelve hours the best one can do is to control the existing infection. After the patient is anesthetized, the wound should be protected with sterile gauze while the adjacent skin is thoroughly shaved and cleaned. The wound itself and any exposed tissue should be gently washed with saline solution, care being taken not to allow the fluid to enter the deeper planes. A strip of skin 0.5 cm. wide is then dissected from the margin of the wound, and the wound is enlarged sufficiently to allow free exposure of the deeper portions. The skin is covered by towels attached to the edges of the wound. With fresh instruments each layer is then carefully attacked until the whole area has been explored. In removing the foreign material and devitalized tissue great care must be observed not to drive the contamination into the depths of the wound. It is unwise, therefore, to restore the structures to their normal position before they and their bed have been thoroughly cleaned. For this reason the practice of reducing compound fractures and carrying out the débridement through a hole in the encasing plaster is to be condemned. In irrigating the wound, large quantities of saline solution should be used. The stream should be made to flow from the depths of the wound outward, with good retraction. If the irrigating can is held high and the nozzle placed in a small wound, the infection can be carried long distances along fascial planes. It is unwise to use any chemicals stronger than saline solution on the raw tissues. It seems foolish to try to remove tissue devitalized by the trauma and then to sear the raw surface by strong chemicals. These may kill some pathogenic organisms, but they also kill human cells.

4. Reduction of Displacements: The plan of controlling the infection first and reducing the fragments later has resulted in many deformities and disabilities. The time for reduction is as soon as the débriding operation has been completed. If this can be accomplished and the reduction maintained the patient will at least have a straight limb of the proper length.

5. Immobilization: Rigid fixation is even more desirable for compound fractures than for simple ones. It not only favors bone repair but helps to control the infection. Frequent movements of the ends of the bone, even through a small arc, tend to tear the limiting wall of granulation tissue and let the infecting organisms invade new tissue. Plaster incasements may be sufficient for transverse fractures without comminution. Openings must be made sufficient to allow dressing of the wound.

For oblique or comminuted fractures single wire traction with suspension in a plaster gutter splint may be used. Some prefer to insert wires above and below the site of fracture and to embed these in a circular plaster splint.

For a number of years I have used internal metal fixation. At first the screws or the plate and screws were applied through an incision separate from the original wound. In recent years, however, they have been inserted through the original incision. The leg or arm is then suspended in a plaster gutter. This method allows whatever treatment of the wound seems desirable, permits mobilization of adjacent joints, avoids constriction of circulation and insures proper length and axis. The hardware usually is removed after it has served its purpose.

6. Treatment of the Wound: The ideal method is to carry out the débridement so early and so thoroughly as to avoid infection, so that the wound may be sutured primarily. Usually, however, some infection is left behind, and if there is tension in the wound it is much more apt to spread and do serious damage than if the secretions find a ready exit. Primary suture is being successfully carried out in many clinics, but the incidence of serious infection, extensive osteomyelitis, amputation and death is higher than when the wounds are left open, at least for a while. Secondary suture or healing by granulation with subsequent skin grafting is safer.

The problem of deciding what is the best subsequent treatment of the operative wound is an interesting one. It is undoubtedly true that frequent, rough dressings with careless technic do more harm than good. It is also admitted that the normal efforts of the body tissues and fluids to resist the invading organisms are of great value. These should be helped and not hindered. Wide experience has shown that the Carrel method does control infection and help to get rid of devitalized tissue. It is my opinion that for compound fractures which can be débrided and immobilized properly within eight hours of the injury and in which the local damage to tissue is not too great, it is better to separate the surfaces of the wound with petrolatum gauze with no tension in the wound and to change the dressings infrequently. When the débridement has been delayed or incompletely carried out it is wiser to use the Carrel method.

CONCLUSIONS

Treatment of compound fractures involves healing of the broken bone and of the injuries to the soft parts and control of infection. The future course depends largely on the character of the original injury, the amount of secondary trauma incident to transportation, the thoroughness of the primary treatment of the wound and the time at which it is carried out. With early débridement, efficient reduction and firm immobilization the type of subsequent treatment of the wound becomes of less importance.

TREATMENT OF COMPOUND FRACTURES

WITH SPECIAL REFERENCE TO MILITARY SURGICAL PROCEDURES

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Traction, reduction, drainage, débridement, wound sterilization and immobilization are terms used in thousands of pages that have been written about the contributions of the great war to civil surgery. Yet these very terms constitute some of the difficulties in dealing with the subject under consideration, for many papers and even textbooks have left the reader in doubt as to their exact meaning. And, too, meanings change as ideas develop. Claims for the so-called new methods and effects of war methods on civil practice underwent considerable change after the war, up to the publication of the Surgeon General's report in 1925.

Overseas experience during the war years revealed to me not only confusion of terms but an unfortunate confusion in principles and in practice. To surgeons with what Sir Robert Jones called an "orthopedic conscience," many methods and technics prevailing during the war were far from satisfactory. It was the practice to treat compound fractures as wounds until healed and then as fractures. Splinting was a compromise in most cases, adapted so that the Carrel-Dakin or some other antiseptic treatment of the wound could be carried out. Prolonged delay in healing of the fracture, as well as deformity and disability, was the result, as hundreds of cases that came under my personal observation testified. There was a surprising return to the mobilization methods of Championniere; even septic joints were kept moving, and disastrous local and general infections resulted. Infected wounds presumably rendered sterile by chemicals were sutured. True, there were a few brilliant primary or secondary closures, but there were also many "explosions." The principle of drainage for infection was forgotten in these attempts to cover up pockets of active or latent septic organisms.

Some of these methods and technics were proposed as new principles. Yet actually most of them violated or disregarded such fundamental principles as immediate reduction of fractures, drainage for infected wounds, immobilization in correct position and control during repair of the fracture. Restoration of circulation and nerve supply and provision for rest to favor physiologic function in injured and inflamed parts were neglected. Apparently it was forgotten that these are absolutely essential for defense against infection and for repair.

Such were the considerations that led me to search for a better program for the treatment of compound fractures in the years just after my military experience from 1917 to 1919. I began with a different method of treatment of osteomyelitis and other infected wounds and in 1923 published an account of the method and results up to that time. The plan was designed to conform to the real fundamentals of fracture treatment. I carried out immediate reduction and instituted and maintained adequate drainage for all compound fracture wounds. For primary traction and permanent fixation I employed plaster of paris with moleskin adhesive plaster, ice tongs or pins. Finally, I protected the wound against trauma and secondary infection during the operative treatment and after-care by avoiding postoperative dressings. This was tried out first in cases of chronic low grade infection, but it was soon found that the patient could defend himself against almost any kind of infection if the surgeon would refrain from the usual custom of traumatizing the surface of the wound and adding new and different organisms by exposure, dressings, instruments and fingers every day.

The program I proposed in 1923 was as follows:

1. Prior to any operation in a case of chronic osteomyelitis or of compound fracture, immobilize the patient on a traction table with all of the injured parts as nearly as possible in correct anatomic position (fig. 1). Reduce the fractures at once, especially by efficient traction, so that circulation and nerve supply are restored. If there is older deformity, correct it first by traction and manipulation. Even in seriously injured patients with multiple fractures or extensive injuries to the thigh, shock may nearly always be avoided by preliminary control of the patient in this way. If a patient arrives at the hospital in shock, employ the customary medication—intravenous dextrose solution, physiologic solution of sodium chloride given hypodermically or blood transfusion. But do not leave him with a mangled limb unreduced and tortured by painful movements and muscle spasm. Efforts to relieve shock (shock therapy) are often futile if the local conditions that cause so much suffering are not relieved.

2. Open the entire infected area and drain by a suitable operation (débridement), so that foreign material and dead or dying tissue are removed. As part of the drainage operation the wound may be wiped out with pure tincture of iodine and alcohol, as in preparation of the skin, in order to reduce the amount and virulence of the accidental infection.

3. To protect the surface of the wound and provide permanent drainage, fill the wound with a nonabsorbent, nonirritating petrolatum pack. (This is the open wound treatment that has prevented gas

bacillus infection and tetanus in so many cases.) Use no drainage tubes, and do not cover any parts of the wound by flaps, sutures or overhanging portions of tissue. The pack must be carried to the depths of the wound, and it must flow over the edges at the top to a distance of about 1 inch (2.5 cm.) on the surrounding skin. This is to carry dis-

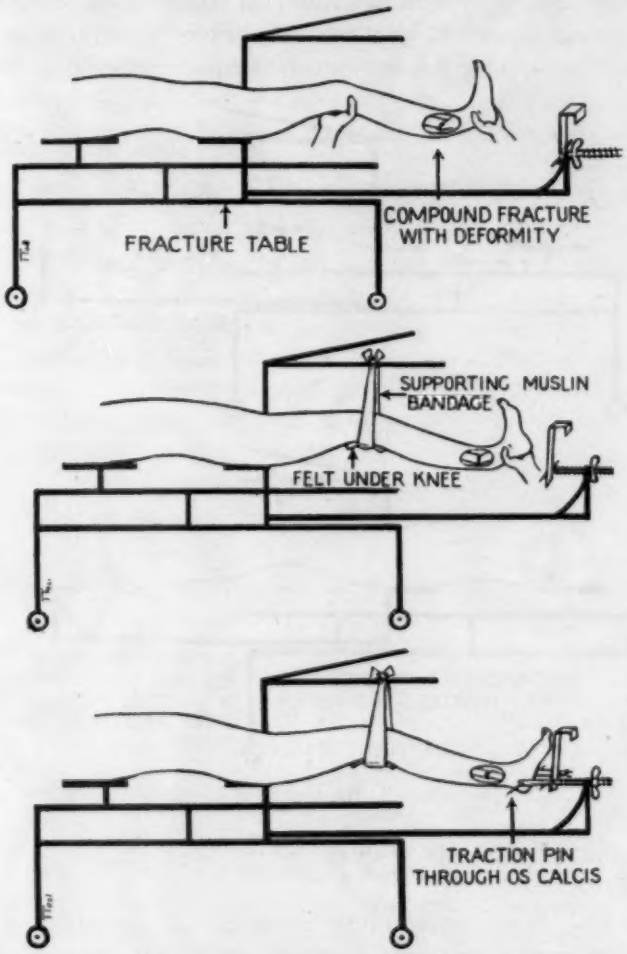

Fig. 1.—Initial stages in the treatment of compound fracture.

charges away from the area just around the wound. Complete the dressing with a dry, sterile absorbent pad bandaged firmly over the drainage pack and its edges.

4. Enclose the entire limb in a plaster of paris cast. In cases of fracture and after the correction of deformities, incorporate in the cast the moleskin adhesive plaster, ice tongs, traction pins or pins extending

directly into the fracture fragments (fig. 2). This makes permanent the traction and fixation obtained on the table during operation. Casts must fit well and be sufficiently extensive to overcome once and for all muscle spasm and irritative motion of all kinds.

5. When removal of a severely injured limb is indicated or even definitely impending, wait, if necessary, for improvement in the patient's local or general condition. But lest this waiting be unprofitable, relieve pain, shock and infection by immobilization of the limb in correct

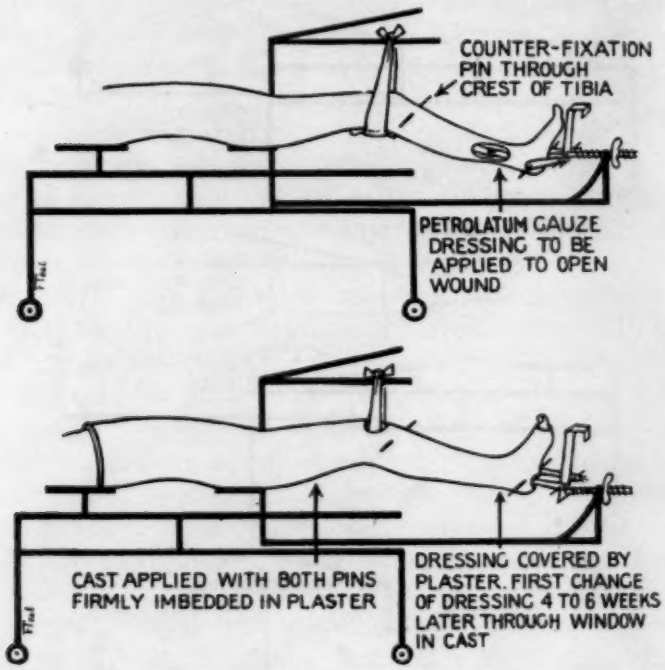
COUNTER-FIXATION PIN THROUGH CREST OF TIBIA
PETROLATUM GAUZE DRESSING TO BE APPLIED TO OPEN WOUND
CAST APPLIED WITH BOTH PINS FIRMLY IMBEDDED IN PLASTER
DRESSING COVERED BY PLASTER. FIRST CHANGE OF DRESSING 4 TO 6 WEEKS LATER THROUGH WINDOW IN CAST

Fig. 2.—Further stages in the treatment of compound fracture.

position and by adequate drainage while other supporting measures are employed.

6. Finally, do no postoperative dressings. If immobilizing devices become inefficient, if discharge is profuse or if odor (because of mixed infection) becomes unendurable, change dressings in the operating room without disturbing the parts and with a minimum of damage to the surface of the wound. Usually the original dressing may remain in place for four to eight weeks or even longer, until the wound has made good progress toward healing.

If such a program is to be adhered to a number of misconceptions must be laid aside.

1. The misconception that "primary treatment must be delayed to allow the patient to recover from shock," hemorrhage or swelling. The fact is that all of these conditions may be prevented or relieved by immediate reduction and control of the injured parts in correct length and position. With reduction of the fracture there is restoration of circulation and nerve supply; hence all of the physiologic functions in the injured part may be expected to improve.

2. The misconception that "every injury is an individual problem to be solved by the particular surgeon attending in each case." This is a general teaching which has done much harm. Adherence to a routine calling for reduction of the fracture and control of the limb will soon convince any surgeon that there are certain rules that are applicable to every case, regardless of time, place or circumstances.

3. The misconception that "plaster of paris cannot be used in the treatment of fractures" because it implies constriction of the limb and will do harm by interfering with circulation. No properly applied plaster of paris cast is tight enough to cause constriction or distress. A painful cast is an improperly applied cast. When a cast including fixation pins has been applied, immobilization in correct length and position is "un fait accompli." On modern traction tables, reduction of the fracture, suitable drainage dressings and a correct plaster of paris dressing with skeletal fixation may all be effected quickly, without difficulty or delay.

4. The misconception that "infection must be combated by active chemical antisepsis" and therefore that splints must be adjustable or removable. It is too often forgotten that Lord Lister, when he introduced the antiseptic method, placed his chief reliance on exclusion of infection from the wound and on the patient's resistance to overcome local and systemic infections. Lister advised repeatedly against the application of phenol and other chemicals directly to the surface of the wound. He warned also against the introduction of infection at the time of dressings and the distribution of infection by metastasis. Frequent dressing, by whatever method, violates the principle of protecting the surface of the wound and the patient against secondary infection. Even such a method as the introduction of maggots every few days subjects the patient to greater risk of mixed infection than does an irrigation or an antiseptic dressing.

5. The misconception that "the wound must be kept clean." As long ago as the time of Ambroise Paré and John Hunter, mechanical cleanliness of the wound was shown to be unnecessary. It is specific infection, and particularly mixed infection, that does the damage in these cases. If the patient can have his original damage and infection minimized by an adequate primary surgical procedure and if he can then be protected

against irritation from movement, muscle spasm and frequent dressings, he will usually be able to defend himself. This is true especially if correct anatomic relations and physiologic function have been restored to the injured extremity.

6. The misconception that "fractures cannot be reduced secondarily or deformity corrected in the presence of infected wounds." During my military service with the British twenty years ago, I was taught that compound fractures must be soundly healed for several months before any surgical procedures could be attempted. Procedures to correct fracture deformities or nonunion and even operations on the peripheral nerves had to wait, not only until healing had been obtained (often it never was obtained) but until the scarred region would withstand a period of massage without "lighting up." Now it is known that under the conditions I have described, that is, drainage when necessary, anatomic reposition, perfect immobilization and protection against infection both at operation and afterward, any of these operations may be done at any time. To do such operations without delay is especially important when control of a fracture has been lost or when deformity is impending or has occurred. In this way long periods of disability and deformity are prevented. Moreover, many patients will heal early, with good limbs, who would go through much longer periods of healing if their deformities and other pathologic conditions remain unrelieved.

My suggestions, including more or less fixed rules for early reduction and the use of closed plaster of paris casts with no opportunity for inspection of the wounds, have aroused some opposition. In some cases the casts became soiled and because of mixed infection had a bad odor.

The use of my methods for military operations was suggested to the Surgeon-General's office almost twenty years ago. At that time their adoption could not be brought about because the plan of treatment was "too much out of line with usual practice."

The years have piled up evidence that the program proposed twenty years ago was sound. I now have documents to show a remarkable success of the method in the military hospitals in and around Barcelona during the Spanish civil war. Trueta [1] reported that in the entire area of which he was director more than 10,000 patients were treated by primary reduction, plaster of paris casts and infrequent dressings. His reports show that the patients treated early in this way were more com-

1. Trueta, J.: Treatment of War Wounds and Fractures with Special Reference to the Closed Method as Used in the War in Spain, London, H. Hamilton, 1939. Dr. Trueta has generously recorded his indebtedness for the methods he used. "In concluding this book, I wish to offer my tribute to Winnett Orr, the advocate of a therapeutic method which is bound to give new direction to surgical practice in its attempt to aid the resistance of the body to infection. He taught surgeons once again to realize that rest is the complement of surgery."

fortable and that they escaped the early septicemias, tetanus and other anaerobic conditions to which such patients with sutured wounds and poorly splinted limbs are subject. He has pointed out also that they endured transportation well and that they recovered sooner and with better limbs. Trueta's [1] personal experience is indicated in table 1.

In commenting on this large and unusual experience, he said:

> I sincerely believe that no other treatment could have enabled us to alleviate for so many victims the horrors of war and air raids. The experience recorded covers thirty months' continuous treatment of war casualties, including the immediate surgical treatment of casualties in 300 air raids. By rapid, properly planned, boldly executed surgery, followed by closed plaster-of-paris casts, the casualties of war can today be spared the torment of having to pass the rest of their days crippled and mutilated. I believe that this is especially true of the victims of air raids if the surgeon is prepared to work in or close to the bombarded area. To the possibility of working under the strain of repeated aerial bombardments my colleagues in Barcelona and I can testify.

TABLE 1 *.—*Results of Treatment of Open Fractures by the Methods Described*

Type of Fracture	Cases	Good or Satisfactory Results	Bad Results	Deaths
Scapulohumeral	55	55	0	0
Shaft of humerus	142	140	1	1
Elbow joint region	64	60	4	0
Forearm	121	110	11	0
Wrist and hand	106	93	13	0
Hip and neck of femur	21	17	2	2
Shaft of femur	101	88	12	1
Knee joint	43	40	3	0
Shaft of tibia and fibula	225	198	25	2
Ankle and hindfoot	67	60	7	0
Forefoot	128	115	13	0
Total	1,073	976	91	6

* Quoted from Trueta,[1] p. 135.

Trueta's figures show better results for such injuries than any previously reported in civil or military practice. One can see that his patients were protected by this plan against the advanced septicemia so often seen in patients when they arrive at the hospital. His experience in the prophylaxis of gas bacillus infections assures me once more that the plan of leaving wounds open is a factor of importance in dealing with all the anaerobic infections. That the petrolatum pack and the cast exclude oxygen from these wounds is, of course, an erroneous idea.

The principle of primary reduction and immobilization in correct position is readily accepted. But if it is proposed to carry out this program by manual reduction and application of ordinary splints, only the experienced and expert surgeon can succeed with the method. Tech-

nics such as delaying of reduction to await subsidence of swelling, suturing of wounds with tube drainage, use of wire splints or split casts, and weight and pulley traction with only sand bags or pillows for splints (all unfortunately still common), are, to say the least, inadequate.

The points for consideration in both civil and military practice are as simple as they are important: For first aid on the battlefield or at the scene of the accident the use of a tourniquet and traction immobilization in a Thomas splint have demonstrated their value as life-saving and limb-saving expedients. Prepared in this way, the patient may be transported safely to a hospital where more efficient traction, débridement, petrolatum pack drainage and fixation in a plaster of paris cast may all be done. This is the plan that I have followed for many years, that is now being employed by many hundreds of surgeons and that was followed so successfully by Trueta at Barcelona.

The same technic is to be applied whether the treatment is primary, that is, applied during the first few hours, or secondary, in the sense that the patient arrives with the fracture in malposition, the wound infected and septicemia and pyemia already established. A restless patient with an unreduced fracture, muscle spasm, pain and a septic wound can do himself far more harm every hour than the surgeon will do by a thirty minute maneuver after which the compound fractured limb will be permanently immobilized in correct position, the wound adequately drained and the surface of the wound and the limb fully protected against further trauma and infection.

Illustrative of the principles and technic we advocate is the following report of a case.

REPORT OF A CASE

D. L. T., a youth aged 19, of Lincoln, Neb., was shot through the right leg while running away from an officer. He sustained a compound, comminuted fracture of both bones just above the ankle (fig. 3 *A*). He came to me twenty-four hours after his injury with the leg in a foot and leg splint. There were considerable deformity and extensive comminution; the wound of entrance was small, but the wound in the front of the leg was large, and a large, loose fragment of tibia was lying with a point protruding when the dressings were taken off. The hemorrhage had been severe and recurred on removal of the dressing.

A traction pin was put through the calcaneum, and the leg was pulled down at once to full length. The leg was lined up as to the foot and knee without much reference to the fracture fragments at first. A second pin was put through the tibia a few inches above the fracture area. The position of this pin is indicated in figure 3 *B*. The exit wound was enlarged slightly, and the large fragment of tibia, which was entirely separated from all tissue attachments, was taken out. Some search of the entire wound area was made for other bone fragments, a few of which were removed, and for particles of clothing that might have been carried in. A considerable number of clots were evacuated. This wound was not packed to the bottom. It was felt that there was a good prospect of rapid healing without extensive packing of the wound. A petrolatum pack was put over the point of

entrance of the bullet, and a partial pack was made of the wound in front with the petrolatum pack extending out over the edges of the wound onto the skin. Iodine was used to clean the entire limb above and below the region of fracture prior to any exploration, but no antiseptic was used inside the wound cavity. There was no established infection, although the patient had a temperature of 100 F. on his admission to the hospital, and this temperature continued to rise slightly for several days. By the fifth day, however, the boy's temperature was normal, and it remained so.

The cast and dressing applied on January 25 were not disturbed until March 9. At that time the cast was removed, the pins were taken out and the wound was dressed. The wound of entrance was healed; the wound of exit in the front of the leg was still slightly open, but there was no inflammation, swelling or

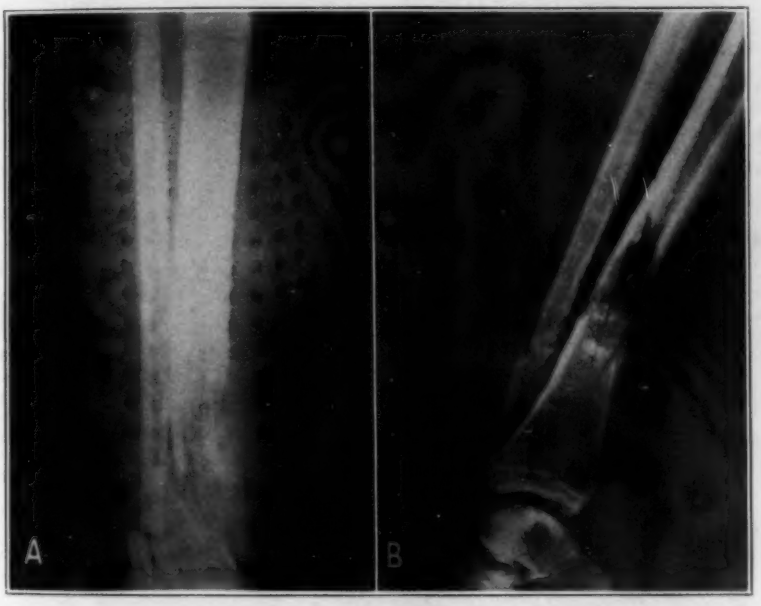

Fig. 3.—*A*, compound fracture of both bones just above the ankle. *B*, position immediately after pin traction and débridement.

evidence of septic complications. The limb was in satisfactory position. A very slight change as to rotation and dorsiflexion of the foot was made without disturbing the fracture area. A new cast was applied above the knee, without pins or fixation otherwise, and this cast was worn for another period of six weeks.

During the second six week period the boy got about a good deal on crutches and, contrary to my instructions, bore some weight on the limb. On removal of the second cast, on April 24, all the wounds were healed and the fracture was firmly consolidated, but because of the weakness of the tibia (indicated in figure 4*A*), a double lateral walking iron was put on below the knee; this was worn until May 20.

The treatment of this patient is described as typical of the kind of treatment that all these patients may have. It is my belief that with less adequate fixation methods and frequent dressings he would have pursued the usual course of a patient with a

compound infected fracture, with all the signs of local and general infection, to which such patients are subject.

Photographs of the limb as of Dec. 30, 1939, eleven months after the original injury, are presented to indicate the kind of recovery obtained by this very simple treatment (fig. 4 *B*).

Trueta's figures are the latest and best statistical results that have been brought to my attention. Many others, however, have made reports indicating a high percentage of recovery in cases of compound fracture and chronic osteomyelitis treated by infrequent dressing.

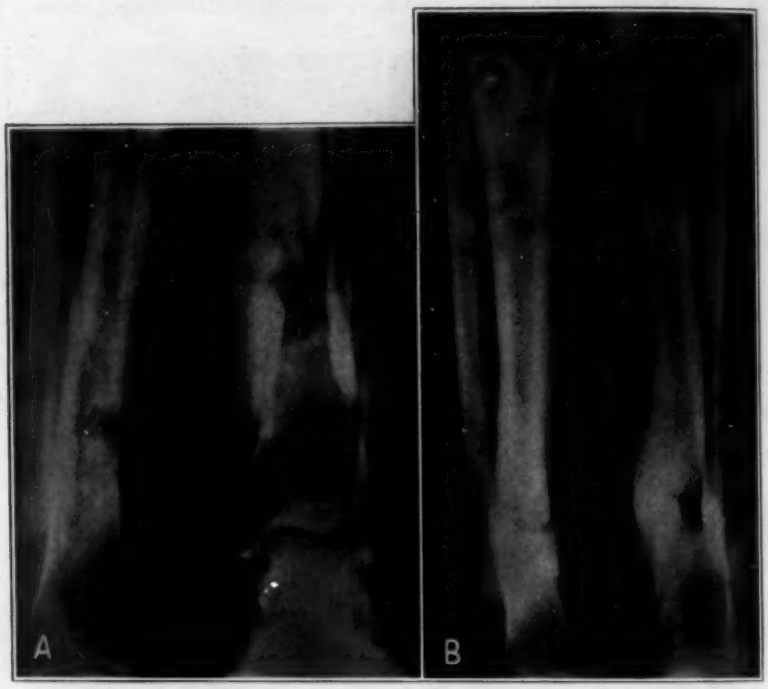

Fig. 4.—*A*, roentgenograms showing defect of the tibia. *B*, roentgenograms taken eleven months after the original injury.

In 1931, Kulowski, then at the Steindler Clinic in Iowa City, made a statistical study of results in cases of chronic osteomyelitis, including compound fractures, from the clinics of Burns at Madison, Wis., Gaenslen at Milwaukee, Steindler and Kulowski at Iowa City and Orr and Thomson at Lincoln, Neb. There were 426 cases, with 358 instances of healing (84 per cent). All of these were treated by the methods described in the present paper. As an interesting comparison, the results of the Baer maggot method at that time showed healing

in 45 per cent of cases (according to the posthumous report of Baer,[2] the final arrangement of which was completed after his death by his associate Dr. George E. Bennett).

During 1932 I made a report on all of my compound fractures up to that time. Of 85 infected fractures, 76, or 90 per cent, were healed;

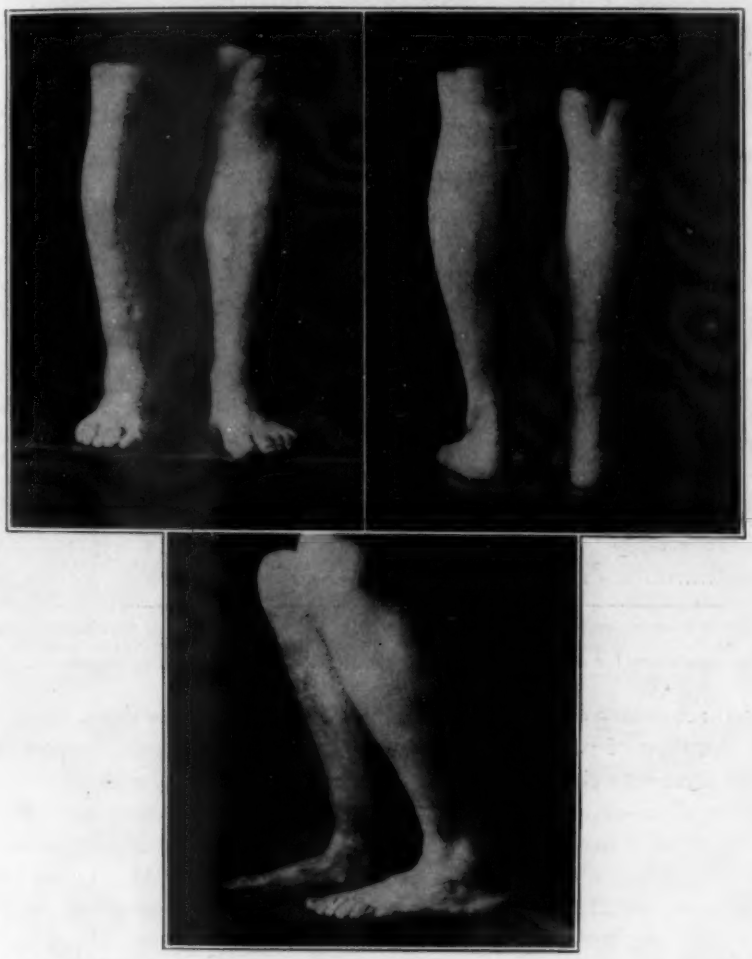

Fig. 5.—Photographs of the patient whose fracture is shown in figures 3 and 4. These photographs were taken one year after injury.

of 183 fractures compounded by operation for deformities and disabilities of various kinds, 100 per cent were healed without infection

2. Baer, W. S.: Treatment of Chronic Osteomyelitis with Maggot (Larva of Blow Fly), J. Bone & Joint Surg. **13**:438-475 (July) 1931.

or failure of union in any case. For compound fractures of all kinds at that time, including those treated by my associate, Dr. Thomson, 268 in all, the results were as follows: Two hundred and fifty-nine were healed; 1 was not healed; 5 amputations were performed, and 3 patients died. The last-cited figures included 84 fractures and fracture infections treated at the Veterans Hospital in Lincoln. Many of these dated from the war days of 1917 and 1918. There were 84 of these; 54 of the patients came to the hospital with unhealed or malunited fractures. Of the 84, 79, or over 90 per cent, entirely recovered.

In 1933, I reported the following cases for one year to the British Medical Association:

There were 6 primary compound fractures, with a total of seven dressings and an average healing time of ten weeks. In the 25 cases in

TABLE 2.—*Summary of Cases and Results*

Dr. Orr Only	Compound Fractures			Good Results and Healing	Poor Results	Results Unknown	Deaths	Total
	Primary	Secondary	Compounded by Operation					
1921 to 1929 (published in Detroit lecture, 1930)	60	98	..	158	1	0	0	158
1929 to 1933 (not published)	86	58	61	187	6	9	3	205
1934 to 1938	6	75	75	131	7	0	2	156
Femurs only, to 1938	14	50	75	127	5	5	2	139
Total	166	281	211	603	19	30	7	658

There is some overlap in cases of fracture of the femur from 1921 to 1938, but such cases are not included in the figures for 1934 to 1938. "Compounded by operation" includes all plastic operations for correction of malunited fractures and leg-lengthening operations.

which secondary operations for compound fracture were done, the average duration of preceding deformity, disability or chronic osteomyelitis or all three was eight months. The fractures all healed, with an average for the 25 cases of three dressings and three months' time for healing.

In 1934 I made a study of 1,300 patients with fracture treated in the city of Lincoln during the years from 1929 to 1933. I had done operations on 212 of these patients. Most of the operations became necessary because of unusual difficulties during or after the primary treatment. Removal of plates or wire or operation for nonunion or infection was necessary in 110 cases. In this series good results were obtained in 96 cases, or approximately 90 per cent. The defect in primary treatment in most of these cases was usually insufficient traction at first or failure to maintain traction in the after-care.

Table 2 is a recapitulation and summary of the various groups of cases referred to. Recent patients, many of whom are well, have not yet been included.

CONCLUSIONS

1. The method of immediate reduction, open drainage, plaster of paris skeletal fixation and infrequent dressing is one which is simple of application either for emergency patients or as a program for secondary surgical care.

2. Reduction of a fracture depends on traction more than on any other factor. Sufficient traction can and should be applied at the time of operation, whether the operation is primary or secondary. Length and position should be maintained by skeletal pins fixed in the plaster of paris cast.

3. Infected wounds at any stage should be left open, not sutured, with the surfaces of the wound protected against trauma and secondary infection.

4. Fracture deformities may be corrected at any stage, even in the presence of local or general infection, if the aforementioned points are observed. All the injured parts are to be restored to correct position, infected wounds all left open, permanent immobilization in correct position maintained and the wound and the injured limb protected against further trauma and secondary infection.

5. The experience of other competent observers, as well as my own, is that good results may be obtained by the infrequent dressing method in 85 to 90 per cent of compound infected fractures of all kinds.

This experience has now been confirmed for military practice in Spain by Trueta,[1] whose observation of more than 1,000 cases in which similar treatment was given yields exactly the same percentage.

TREATMENT OF COMPOUND FRACTURES

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First aid should be directed immediately toward reduction of the fracture by traction, protection of the wound with sterile gauze and splinting with plaster, steel or wooden splints.

On the patient's admission to the hospital, anteroposterior and lateral roentgenograms are made.

OPERATION

Sterile gauze is placed in the wound; the surrounding skin is shaved and thoroughly cleansed with soap, water, ether or benzine. The gauze is then removed from the wound, and an adequate débridement of the devitalized skin, fascia, muscle and detached bone is made. The débridement is of the greatest importance and should be done thoroughly. Wounds compounded from within are usually not as severe as those received from without, nor is the contamination as great. The fracture is then reduced and immobilized by splinting, and the Carrel method of treatment of the wound is instituted at once.

REDUCTION OF FRACTURE

Manipulation and manual traction should be attempted with external fixation, preferably plaster. If internal fixation with plates and screws is used a Thomas, Jones or Cabot splint gives complete satisfaction in selected cases. Molded plaster casts rather than circular casts should be used unless the latter are split within twelve hours, because of the possibility of complications due to constriction or gangrene. Repeated inspections should be made, and at the first sign of circulatory disturbance the splints should be released.

Should the reduction not be satisfactory an open reduction can be done after the local swelling has subsided and the temperature and pulse have become normal, which is usually at the end of ten or twelve days. The operative incision for fixation of the fracture with plate or screw is made not at the site of the original compound wound but at a point opposite, so as not to contaminate this particular field with the operative incision. The compound wound is permitted to granulate and is usually cicatrized before bony union has taken place. However, should a small sinus persist the plates and screws are removed and the wound closed.

WOUNDS COMPOUNDED FROM WITHOUT

Wounds compounded from without should be treated as potentially infected, a thorough débridement being performed at the earliest possible moment. The wound should remain open, and Carrel tubes should be inserted to every cavity and recess. Immediately after the operation the wound should be copiously irrigated through Carrel tubes with solution of sodium hypochlorite. At the end of two or three days the dressings are changed and new tubes inserted.

FIXATION OF FRACTURES WITH METAL

For the past thirty years I have used steel fixation routinely wherever indicated. Steel plates and screws are usually employed for transverse fractures and transfixion screws for spiral and oblique fractures. In selected cases, extensive comminuted fractures can be treated by bridging the site of fracture with long plates. Skeletal traction with Kirschner wires incorporated in the plaster is used occasionally but not as a routine procedure, because the introduction of pins or wires above and below the site of fracture increases the possibility of complications arising from the use of this technic. When indicated it is a perfectly justifiable procedure, but it should not become the method of choice to the exclusion of other recognized procedures. Extensively comminuted fractures do not usually lend themselves to fixation by screws and plates and should be treated by skeletal traction, preferably by Kirschner wire. If reasonable reduction can be secured with plates, traction by Kirschner wire is not necessary.

It is the general consensus that metal plates and screws are contraindicated in the treatment of compound fractures. Unless débridement and the Carrel wound sterilization are done thoroughly, plates and screws should not be used, as they tend to complicate the massive osteomyelitis which frequently results from infection. As a rule, if plates and screws are used the wound should be left open. It is admitted that in some cases in which there is little or no swelling or trauma to the soft parts closure of the wound can be done after internal metallic fixation, but such treatment should be undertaken only by surgeons of wide experience and sound judgment. If the slightest evidence of infection becomes manifest, the wound should be widely opened, plates and screws exposed but not removed and the Carrel method instituted, it having been made sure that the tubes have been inserted in every pocket or recess. It is extremely hazardous to use metal fixation in compound fractures unless the wound has been carefully débrided and the Carrel treatment instituted immediately. The theoretic objections to the use of metallic substances in compound fractures are based on faulty and incorrect conclusions due to inexperience and opinions handed down before the

acceptance of débridement as a fundamental principle and the Carrel technic as a definite prophylaxis against infection.

For the past thirty years, vanadium steel has been used in plates and screws because of its great physical and metallurgic properties. When exposed to sodium hypochlorite, these steel plates corrode, and as a result of the oxidation due to the deposit of ferric oxide staining takes place. As a result, 60 per cent of the plates and screws used in compound fractures must be removed. I usually remove plates and screws if the wound is unhealed in five to seven weeks after insertion of the foreign bodies.

The objections to vanadium steel have been overcome recently by the production of a new stainless steel (chrome, 18 per cent; nickel, 8 per cent; molybdenum, 2.38 per cent; Rockwell hardness, C scale, 35 to 37), which has all of the physical properties of vanadium steel and will not corrode in the presence of sodium chloride or sodium hypochlorite solutions. It is much superior in physical properties to vitallium, which is objectionable because it is cast metal, is entirely too brittle and contains air bubbles. This new alloy steel is the solution to the question of the use of metals where screws, plates, nails and other metal fixative devices are used. Should they be removed, they can be used again. Metals such as monel and duralumin should not be used because of the tendency of the copper in the monel metal to corrode and because duralumin likewise has a tendency to corrode and effloresce in the presence of saline solution. Electrolysis does not occur when like metals are used.

CONCENTRATED SOLUTION OF SODIUM HYPOCHLORITE AND SODIUM CHLORIDE (HYCLORITE N. N. R.)

Sodium hypochlorite (bleaching lime) has long been known as a powerful disinfectant and deodorant. Semmelweis' epochal discovery is well known to any one familiar with the story of antiseptics. Many hundreds of antiseptics, too numerous to mention, have been advocated for prevention of wound infection as well as for treatment of infected wounds but have been proved absolutely worthless when put to a clinical test. The action of an antiseptic in a test tube or Petri plate is entirely different from that of an antiseptic in actual body wounds.

In the early years of the World War (1914 and 1915), every antiseptic known at that time was tried both to prevent wound infection and to control it when once present, without success. Carrel and his co-worker Dakin again reverted to the use of sodium hypochlorite, but because of its instability when exposed to air it was necessary to have a lime of known chlorine activity in order to make a 0.5 per cent solution of sodium hypochlorite. The solutions were unstable and more or less

caustic, necessitating frequent titrations and the making of a fresh solution every few days. The solution, while strongly antiseptic, was absolutely nontoxic, and a solvent of necrotic tissue did not destroy living cells or tissues. Liquefaction by oxidation of necrotic tissue removes from the wound the culture mediums on which many bacteria thrive.

In 1918, an electrolytic process was evolved in the manufacture of a concentrate (sodium hypochlorite 4.05 per cent and sodium chloride 3.25 per cent) of low alkalinity, p_H 11. This solution is relatively stable, losing approximately 10 per cent active chlorine per year. Its use has greatly simplified the Carrel treatment in that it eliminates the daily titrations and the making of a solution every few days. The addition of 6½ parts of water to 1 part of the concentrate makes a solution of proper strength as to both sodium hypochlorite and sodium chloride content and is vastly superior to solutions made from sodium hypochlorite or liquid chlorine. The commonly used term "chlorinated soda" does not sufficiently specify the nature, quality or content of sodium hypochlorite. This concentrate when diluted 6½ to 1 is hypertonic, greatly increasing osmotic action and the flow of phagocytes and lymphocytes into the wound, and there is no danger of dehydration of the body, such as is produced by salt packs with the technic of Sir Almoth Wright. One frequently hears that the same results can be secured with physiologic solution of sodium chloride. Such statements are based on lack of knowledge of chemistry and of the physiologic action of sodium hypochlorite and on inexperience so far as the technic of Carrel is concerned. The incidence of infection in time of peace should be practically nil. The environment, the nature of the wounds and the presence of foreign material (multiple shell fragments, soil and clothing) do not permit as careful asepsis in war as in peace. However, the standardization of treatment from "firing line to base" in the British Army at the Salonika front from 1915 to 1918 (débridement, sodium hypochlorite irrigation, etc.) tremendously reduced the mortality and the number of amputations and wound infections. A visit to the clinic of DePage at LaPanne, Belgium, disclosed 80 compound fractures undergoing treatment without a single infected wound. Sepsis and infection of wounds were completely controlled in injuries treated within the first six to eight hours. Visits to every other hospital, except for three where the Carrel method was carried out, revealed infection in every compound fracture (May to November 1916).

A most scrupulous instrumental technic and most careful asepsis with attention to sound and generally accepted surgical principles must be adhered to if success is to be assured. The principles are simple and can be easily executed by surgeons and nurses who have received instructions, who have an understanding and who are intent on carrying out the technic without alteration.

NONUNION FOLLOWING COMPOUND FRACTURES

Nonunion is a more frequent complication in compound fractures than in simple fractures, but it is important that it be differentiated from delayed union. Application of an autogenous bone graft, either inlay or onlay, is usually the treatment of choice. The graft should be firmly affixed to the host and immobilized by transfixion with two to four stainless steel (chrome-nickel-molybdenum) screws.

After operation, plaster splints completely immobilizing the fracture should be used until union occurs. The Morton Smart technic of graduated contraction of muscle should be instituted as soon as union takes place, as it not only restores muscle tone rapidly but increases the circulation to the extremity.

If postoperative infection occurs, the wound should be opened widely and Carrel tubes inserted into every recess and cavity, the hypochlorite solution being injected every two hours until the wound is free from gross infection. Infected wounds usually cicatrize, leaving one or more sinuses leading to the steel screws. This is due to corrosion or oxidation of the steel. After union has taken place, the screws can readily be removed. When the initial treatment of careful débridement and the Carrel technic with hypochlorite solution has been properly done, postoperative infection seldom occurs, as one is operating in a field that has been noninfected.

If osteomyelitis or infection has complicated the healing of a compound fracture, resulting in nonunion, the bone-grafting operation should be delayed from six to twelve months. Despite delay in grafting, infection not infrequently follows in cases in which chronic osteomyelitis and infection have existed for a long time. The clinical appearance is normal, and one is apt to find evidence of walled-off infection in small foci which are activated by the operative procedure, resulting in the failure of the bone-grafting procedure. Repeated bone grafts, two and sometimes three, are necessary in these cases before strong bony union is secured. The prolonged convalescence could have been materially reduced had the initial treatment of débridement, immobilization and the Carrel method been instituted.

CONCLUSIONS AND RESULTS

Since January 1917, a period of twenty-three years, the treatment of compound fractures by débridement, with the Carrel technic, reduction of the fracture by internal or external fixation and immobilization has been standardized in this clinic. There were treated a total of 11,127 compound fractures (not inclusive of traumatic amputations and fractures of the skull, chest or pelvis), of which 630 were fractures of the long bones, with the following results:

One amputation of the leg due to loss of soft parts. One third of the shaft of the tibia had been destroyed at the time of the accident.

Three amputations of the leg due to thrombosis and secondary hemorrhage, with extensive destruction and crushing of the bone and soft parts. Despite gross trauma, an attempt was made to avoid amputation, to no avail. In all 3 of these cases the leg should have been amputated at the time of admission.

One amputation due to frank infection.

Eighteen amputations of phalanges due to destruction of blood supply and loss of soft parts.

No cases of sepsis.

Two deaths, one from an embolus a few days after admission and the other from shock following a reconstruction operation.

The results secured are ample evidence of the soundness of the principles employed. I am not in accord with the methods being advocated in Europe of nonpadded plaster, closed technic of treating compound fractures. I fully realize that such methods may be necessary as a war emergency. However, when time and environment permit accurate reduction of the fracture, débridement and the Carrel technic with immobilization either by plates or by splints is the best procedure and is certain to bring about the best functional results in the shortest period, with a minimum of deaths, sepsis and amputations.

COMPOUND FRACTURES

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The present treatment of so common an affliction as a compound fracture has to a certain extent reached a fixed stage. As with any fracture, factors (such as shock, hemorrhage, or cerebral injury) which threaten the life of the patient must be attended to before anything more than immobilization of the fracture by the simplest means is attempted. Ideal débridement with immobilization until union has occurred is recognized as utopian. The proper technic of débridement, however, and the proper treatment of the wound after débridement are still points of debate, and it is these points which are to be investigated in this study. Numberless essays have been presented dealing with the treatment of compound fractures, each citing the method particularly favored by the writer, with a list of his favorable results as supporting evidence of the superiority of the method discussed. These authors vary from those who would recommend sewing the débrided wound layer by layer, tightly, as a clean wound, and those who would recommend irrigation of the open wound with a chlorinated solution designed to dissolve dead tissue to those who would pack the débrided wound wide open with petrolatum gauze and allow the pack to be extruded from the base of the wound by the advancing walls of granulation tissue. Such diversity of opinion not only indicates the lack of an entirely satisfactory method but emphasizes that whatever the method is, it is good in the hands of those who are familiar with its technic.

The healing of broken bones is in itself a problem so complex and so strikingly influenced by accessory factors that in general it has no immediate place in this paper. However, in so far as factors which present themselves in compound fractures influence wound healing and bone healing, a discussion of these contributory factors is important. The outstanding factor is infection. This investigation is an attempt to

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evaluate certain ideas in regard to treatment of compound wounds, especially those sustained in dirty surroundings. That other interesting associated facts present themselves in analysis is assumed.

PROBLEM AND SOURCE OF MATERIAL

The specific aim of this analysis is to investigate the incidence of wound infection in compound fractures in two groups of cases. One group was treated by thorough sharp débridement, followed if necessary by cleansing of the interior of the wound with copious floodings of bland solutions, such as saline solution or soft soap U. S. P. (green soap) followed by saline solution. For the second group almost the same routine was utilized, the difference being that iodine and alcohol were introduced into the depths of the wound after it had been débrided, before closure and sometimes before débridement.

The material studied consisted of the rank and file of compound fractures observed in the "male fracture ward" of the Cook County Hospital. A few cases were not included because they were classified under another heading; the cases of a few women and children are included because the patients were cared for by the resident surgeons from the "male fracture ward." The number of cases was 131. The details of treatment were almost identical. The fracture was temporarily splinted, and the patient was examined for associated injuries. Such factors as hemorrhage, cerebral injury and shock, which might jeopardize the life of the patient, were treated; it was not until treatment of the fracture was deemed imperative or safe that the injured member was given definitive care. At that time the palpable distal pulses were investigated, the viability of the distal part assayed, the fracture studied and the most feasible means of immobilizing the fracture considered. Anesthesia was induced (most often ether anesthesia or local anesthesia in this series) and the extremity unsplinted. The compound injury was then covered with sterile dressings, and the entire surrounding skin was cleansed, shaved and painted with iodine and alcohol up to the cutaneous margins. After the field was draped as for a major surgical procedure, the most gross foreign material was picked out of the interior of the wound. Then with a sharp scalpel a rim of skin was excised from the edge of the wound, and the underlying soft tissues were removed en bloc as sharply as possible, the instruments used being changed several times in order to minimize contamination of the freshly produced surfaces. Nothing except indispensable tissue, such as tendons, blood vessels and nerves, was spared. The bone itself, if dirty, was scraped or washed. Bony fragments, if freed from all tissue, were lifted out of the wound. Gross hemorrhage was arrested by ligation of bleeding points. The wound was then closed with the idea of accomplishing layer by layer approximation without such tight

closure that wound secretions would accumulate or that postoperative swelling would produce necrosis. The skin was usually closed by silkworm gut, with a surgeon's knot, which could be manipulated at each dressing to accommodate the state of the tissue swelling.

Although it was not possible to expose the closed wounds to the air, every attempt was made to maintain dryness of the wounds and in particular to change the dressings when the serosanguineous discharge was sufficient to keep the dressings moist. This had a twofold purpose: (1) to prevent retrograde infection from cutaneous saprophytes into wet dressings and thence into the wound and (2) to utilize the capillarity of the dressings to remove undesired accumulations of fluid beneath the edges of the skin. As soon as a solid crust had covered the edges of the skin, the dressings were removed and the wound allowed to remain exposed to the air.

In the cases in which iodine and alcohol were introduced into the wound, the aforementioned technic was used except that the débrided wound was either painted or flushed with these drugs. Such devices as relaxing cutaneous incisions and incisions for counterdrainage were used as needed. In no case were packs inserted into the wound. In 1 case Dakin's treatment (with diluted solution of sodium hypochlorite U. S. P.) was started but was abandoned soon. In a few cases there was such loss of tissue that primary closure was impossible.

Before progressing to the discussion of statistics, it should be emphasized that no two cases are similar and that even in a relatively large group, such as this one, there are enough varied factors almost to nullify the value of comparison of the therapeutic methods. There are rarely two wounds in the same region of a bone with equal amounts of comminution, equal amounts of contamination and an equal amount of damage to the blood supply. The final outcome is also influenced by such factors as the age and general health of the patient and his ability to withstand the shock of the accident. The last-mentioned factor is rarely adequate in the average patient who presents himself for care at the Cook County Hospital.

STATISTICS CONCERNING FRACTURES

The general distribution of the fractures in this series of 131 patients was as follows:

Ninety-three, or 70.9 per cent, were fractures of both bones of the leg.

Eighteen, or 14.2 per cent, were fractures of the humerus and forearm.

Ten, or 7.6 per cent, were fractures of the hand.

Seven, or 5.3 per cent, were fractures of the femur.

Two, or 1.0 per cent, were fractures of the patella.

One, or 0.7 per cent, was a fracture of the olecranon.

From a different point of view, especially in regard to further analysis, the fractures in the 131 cases were studied with regard to the following facts:

There were 31 deaths.

Six patients came in six to eight days after injury, having been treated elsewhere; 3 of these were infected.

Six patients signed a release and left the hospital.

Eighty-eight patients lived and were finally dismissed from the hospital. Half of this number were treated with iodine in the wound and half without.

Deaths.—Perhaps the most startling figure is the high number of deaths. In the following list they are classified as to cause. These being traumatic are coroner's cases, and the patients are usually signed out under the blanket diagnosis of "shock and hemorrhage," with no autopsy.

Death terminated 31 of 131 cases (24.2 per cent).

Ten deaths were from shock or cerebral injury (within twenty-four hours).

Seven were from delayed shock, bronchopneumonia, etc.

Three were from delirium tremens.

Three were "anesthetic deaths."

Two were from internal hemorrhage.

Two were from gas gangrene.

One each was due to "pulmonary embolism lobar pneumonia," post-operative intestinal obstruction and accident.

Probably in the first group of patients death was inevitable, and only because of the efficiency of the police force in bringing seriously injured patients to the hospital on discovery did the patients live long enough to enter the ward. The second group of patients were those who never satisfactorily rallied from their original injury and within a week, or perhaps less, slipped, became semicomatose, had bronchopneumonia and died. In this group there was 1 patient who died of wound infection. He was admitted to the hospital only four hours after his accident but with unmistakable signs of sepsis, the edges of the wound being reddened; he already had fever and presented an exhausted appearance. He lingered six weeks before death. There were 2 cases of gas gangrene; both of the patients were severely injured. One of them was treated with iodine and the other without. Both died after amputation of the contaminated extremity. The group of cases of internal hemorrhage and "anesthetic death" is embarrassing. The 2 patients with internal hemorrhage seemed clinically to have a crushing wound of the chest with massive intrapleural hemorrhage. One of the "anesthetic deaths" occurred in a man aged 50 who had a fractured humerus. His death was sudden, occurring during the first whiffs of the anesthetic.

The symptoms were interpreted as indicating an attack of coronary occlusion. The other 2 patients were men with severe injuries to the leg who presumably had more cerebral injury than was apparent clinically. There were 1 patient who died suddenly of pulmonary embolism on the second day of hospitalization, 1 with lobar pneumonia, and 3 who suffered from delirium tremens. Two of the last-mentioned patients had suffered from severe injury, and the psychotic episode developed within twelve hours after injury. In these cases the diagnosis of fat embolism might have arisen. In 1 the fundi did not show evidence of fat emboli. The patient in the third case was a man with a compound fracture-dislocation of the ankle, whose symptoms developed twenty-four hours after injury and who died within six hours after their appearance.

It is interesting to note the following distribution of the 31 deaths according to fracture.

Twenty-six, or 83.6 per cent, of the patients who died had fractures of both bones of the leg.

Three, or 9 per cent, had fractures of the femur.

Two, or 7 per cent, had fractures of the arm.

The mortality rate for the various fractures is indicated in the following data:

Seven were fractures of the femur, with 3 deaths (42.8 per cent).

Ninety-three were fractures of the leg, with 26 deaths (28.0 per cent).

Eighteen were fractures of the arm, with 2 deaths (7.0 per cent).

Infections.—On this subject, which is the main point of interest of this paper, we present the following statistics, based on the cases of the 88 patients who survived and finally left the hospital. In patients treated without iodine and alcohol, infection occurred in 6, or 13.1 per cent; with iodine in the wound, it occurred in 8, or 18.1 per cent—a slight difference, since the numerical case difference is only 2. However, of the 31 patients who died, there were 11 whose wounds showed evidence of infection. In 2 of these there was definite gas gangrene. One patient (mentioned previously) died from his infection. The other 8 showed varying amounts of infection, in most cases interpreted as resulting at least in part from the patient's general debility, since all infections (excluding gas gangrene) occurred in that group. In addition to the 11 patients who died of infection, there were 14 who survived.

Of the total of 25 patients with infection, 21, or 84 per cent, had fractures of both bones of the leg; and of 11 patients who died, all had fractures of both bones of the leg.

Comparison of the average number of days in the hospital for the patients with clean and for those with infected fractures shows a much longer stay for the infected patients. Including infected patients, the average number of days in the hospital was forty and three-tenths in the group which was not treated with iodine and alcohol in the wound and fifty-six and five-tenths for the group treated by this method. For the infected patients alone, however, the number of days in the hospital was respectively eighty-six and eight-tenths and eighty-one and five-tenths. Without much difference in the two groups, the number

Detailed Analysis of Cases in Which Fractures Were Treated in the Hospital

Without Iodine	Factor Considered	With Iodine
44	Number of cases (total)	44
40.3	Average number of days in hospital (total)	56.5
6	Cases of infection (total)	8
13.1	Percentage of infected wounds	18.1
86.9	Percentage of clean wounds	81.9
86.6	Average number of days in hospital	81.5
2	Number of fractured femurs	2
0	Number of infections	1
28	Fractures of both bones of the lower part of the leg	30
39.9	Average number of days in the hospital	67.5
5	Number infected	6
18.0	Percentage infected	16.6
100.6	Number of days in hospital (infected)	101
36.6	Number of days in hospital (clean)	40.5
17	Cases in which a Steinmann nail was used	26
60.0	Percentage nailed	80.0
13	Number of cases of fracture treated with a nail, clean	20
82.0	Percentage nailed, clean	76.0
39.5	Number of days in hospital, nail, clean	66
5	Number of cases of fracture treated with a nail, infected	6
18.0	Percentage nailed, infected	16.6
100.6	Number of days in hospital, nail, infected	102
10	Number of case immobilized with plaster	6
35.0	Percentage treated with plaster	20.0
36.5	Number of days in hospital with plaster	40.5
0	Number of infections with plaster immobilization	0

of days in the hospital was practically doubled with the development of infection. The duration of hospitalization is admittedly long. We were forced to hospitalize some who might have been treated as outpatients because we could not depend on them to return to the follow-up clinic.

Patients Treated Elsewhere.—For the 6 patients who were not given primary treatment by us the rate of infection was 50 per cent. These patients came in from six to nine days late, often with packs deep in the wound, no débridement and inadequate immobilization. One had mild gas gangrene and recovered after multiple incisions and potassium permanganate dressings.

Type of Fracture.—It is noted from the data presented earlier that a majority of the fractures were fractures of both bones of the leg. Their

number alone justifies their being considered separately, but their importance is even greater because of the difficulties of obtaining satisfactory limbs in these cases. Such injuries are often contracted by direct violence from an automobile accident, especially from bumper injuries. The tibial crest is subcutaneous and easily injured; the fracture is very easily compounded, and, since the accidents occur in the street, usually the contaminating materials are the worst. Add to that the recognized difficulty in covering the fractured tibial crest with viable tissue (particularly after loss of tissue) which will not slough on tension and the known sluggishness of tibial fractures in developing adequate callus, and their importance pyramids.

In discussing these cases it should be noted that there was no rule which decided the method of immobilizing the fracture. The choice as to whether a Steinmann nail was used depended on the judgment of the resident surgeon. It may be noted that 60 per cent of the fractures treated without iodine were treated by skeletal traction, while 80 per cent of those treated with iodine were so treated. This, no doubt, added to the number of days in the hospital for the latter group. As conditions varied it occasionally became necessary to change from primary immobilization in plaster to skeletal traction. In none of the cases in which immobilization in plaster was used throughout did infection occur. This may be explained either because the size of the compound injury was slight or because frequently with the development of infection the treatment was shifted to skeletal traction.

Steinmann Nail.—In this group there were 3 infections about Steinmann nails. No nails pulled through the os calcis.

Interval Before Treatment.—Another important factor is the interval between injury and débridement. After attempting to classify these cases, we finally arrived at the conclusion that there is a fair chance of obtaining a clean wound if the patient is treated within eight hours after injury. We observed several wounds which were clean and which were débrided for the first time twenty-four hours after injury; 1 death occurred in a case in which the patient was seen within four hours after injury. In this case the wound seemed infected on entry. In the group which came in late (twenty-four hours to nine days) the percentage of wound infection was 50 and would undoubtedly have been higher had not some of the patients been given good care elsewhere.

Gas Gangrene.—There were 3 cases of gas gangrene; 2 of the patients died. In the cases of these 2 there was only a short interval between the injury and the development of severe signs of sepsis. The third patient entered the hospital late, with mild symptoms of sepsis; gas gangrene was detected, but he recovered.

Size of Cutaneous Defect.—The size of the exposed wound is a terrifying factor at times. More important than the size of the cutane-

ous opening is the extent of internal avulsion of the tissues. If the periosteum is avulsed from the bone; if the bone is fragmented; if the vessels are torn and occluded and the entire wound crushed, these factors outweigh the size of the cutaneous injury. There were 2 patients listed here as infected who were interesting from this point of view. Both presented themselves with severe comminution and avulsion of the periosteum of the tibia, with great loss of tissue. In 1, some 14 inches (35.5 cm.) of tibia was denuded of periosteum and surrounding muscle. The legs were cleansed, débrided and immobilized with skeletal traction. For fourteen days the patients showed no signs of infection, no fever and no discharge. At the end of that time, however, a slight increase in the amount of serous discharge from the open wounds was noted, and finally, after three days, the discharge became frankly purulent. Even then the patients had no fever, and the infection did not spread beyond the confines of the exposed bone. Later, in the exposed marrow cavity, granulation tissue could be seen filling the cavity, and it also sprang from the viable bone. Still later, large pieces of bone became loose, and the avulsed periosteum laid down new bone. Our explanation was that the wound had been clean after débridement; had we been able to close the skin or had the injury not been compounded, the bony fragments would have been absorbed and replaced with no ill effects. However, in these open wounds the dead bone, acting as a foreign body, eventually had become secondarily infected.

Follow-Up.—We have a saying that "only the bad results come back," but it is hard to believe that the percentage of good results is as high as such an interpretation would indicate. A more satisfactory follow-up might throw light on such important questions as final results and the influence of infection on callus formation. Unfortunately, the percentage of follow-up in these cases was too low to allow formation of definite conclusions as to the final results.

COMMENT

A wound which can be débrided properly is a wound which has been seen as a contaminated and not yet infected wound. Careful excision of all contused tissue and removal of foreign material are done, the aim being to convert the area into a clean surgical wound. However, once contamination has occurred, it is doubtful that any débridement, however careful, can be ideal. One must picture a few lurking organisms in the depths of the wound. Nevertheless, the body tissues are in direct contact with the center of the wound; the tissue juices can pour into this area, and in the absence of necrotic tissue the local defensive mechanisms may attack these organisms and then allow normal healing of the wound to occur.

We base our avoidance of powerful antiseptics in the depths of the wound on a fact of comparative anatomy. In man the skin is able to withstand external trauma and has taken over the ordinary protective functions of the rest of the body. As would be expected, the underlying tissues, relieved of the necessity of protecting themselves from external violence, have diminished powers of self preservation and hence cannot tolerate contact with powerful antiseptics which do not harm the skin.

Picture, then, a wound after careful débridement to which one has added application of iodine and alcohol. Alcohol is an excellent tissue coagulant, and this mixture of iodine and alcohol lines the wound with a layer of coagulated tissue proteins. Adding iodine and alcohol does not sterilize the interior of the wound; it injures the walls of the wound, and the bodily defenses now have to handle the layer of dead cells lining the cavity as well as to attack the organisms in the wound. The organisms, on the other hand, find themselves protected from the bodily defenses by the coagulated tissue and have time to gain a foothold. Such an apparently slight factor may decide whether the wound will remain clean.

SUMMARY

A study of 131 consecutive compound fractures has been made. There were 31 deaths. A detailed analysis of 88 cases is presented; in 58 there were fractures of both bones of the leg, and in only 4 were there fractures of the femur. Immobilization was secured by Buck's extension, plaster or skeletal traction with Steinmann nails. It is felt that if the patient is seen within eight hours after injury a fair chance for effective débridement is offered. Adequate débridement should remove all foreign material and dead tissue, sparing only indispensable tissues. In half the cases the débrided wound was flooded with iodine and alcohol before closing; in half it was not. In 18.1 per cent of patients treated with iodine and alcohol, infection developed; in 13.1 per cent of those treated without iodine and alcohol, infection developed. In the group treated with iodine and alcohol, hospitalization extended over fifty-six and one-half days for uninfected patients and eighty-one and one-half days for the infected group. In the group treated without iodine and alcohol, hospitalization lasted forty and one-half days for the uninfected and eighty-six and one-half days for the infected patients. The comparison of days of hospitalization in the cases in which infection occurred is probably not of much significance, because of the importance of the resultant osteomyelitis in the duration of the therapy. As has been stated, our analysis shows a definitely greater incidence of infection in the wounds treated with iodine. This is explained on the assumption that the use of iodine resulted in the death of a sufficient number of cells to encourage infection.

COMPOUND FRACTURE THERAPY AT THE BOSTON CITY HOSPITAL

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In 1937 I published a paper on the treatment of compound fractures.[1] That paper was based on the work done during the period from 1924 to 1934, whereas this paper covers the work done exclusively in the bone and joint service of the Boston City Hospital during the period from 1934 to 1939. Naturally, a considerable part of the earlier paper is incorporated in this one.

During the five year period from July 1, 1934 to July 1, 1939, there were 12,230 patients with fracture admitted to the Boston City Hospital as requiring "house" care. This number does not include the many hundreds of patients with fractures of the "immediate ambulatory" type treated on the accident floor or in the outpatient department. Of the 12,230 hospitalized patients, the bone and joint service treated 4,491, of whom 398 had the "open," or compound, type of fracture. It is the management of this type of fracture which I shall discuss.

Before I go into the actual discussion of compound fracture therapy, I shall present some data which I garnered from the records of these cases.

GENERAL DATA

Age Distribution.—The age incidence was as follows:

1 to 10 years	10 per cent
10 to 20 years	17.1 per cent
20 to 30 years	10 per cent
30 to 40 years	12.7 per cent
40 to 50 years	19.2 per cent
50 to 60 years	17.7 per cent
60 to 70 years	9.3 per cent
70 to 80 years	4 per cent

Skeletal Distribution.—The fractures occurred in the following bones (listed in order of percentage):

Both bones of the lower part of the leg	28 per cent
Both bones of the forearm	13.5 per cent
Fingers (phalangeal)	10.3 per cent

1. Hermann, O. J.: Treatment of Compound Fractures, New England J. Med. **217**:909, 1937.

Ankle	9.5 per cent
Femur	6.4 per cent
Tibia	5.3 per cent
Toes	4.8 per cent
Thumb	4 per cent
Humerus	3.9 per cent
Metacarpal bones	3 per cent
Wrist	2.5 per cent
Ulna	1.5 per cent
Olecranon	1.5 per cent
Os calcis	1.1 per cent
Metatarsal bones	0.8 per cent
Nose	0.8 per cent
Skull	0.8 per cent
Elbow	0.5 per cent
Radius	0.5 per cent
Astragalus	0.5 per cent
Patella	0.2 per cent
Ilium	0.2 per cent
Tarsal scaphoid bones	0.2 per cent
Spine	0.2 per cent

Causation.—It was interesting to note that 20 per cent of the patients had multiple injuries, of which about two thirds were caused by the automobile.

The causes of fracture were as follows:

Automobile accidents	37.7 per cent
Falls	36.2 per cent
Crush injuries	23.2 per cent
Miscellaneous injuries (caused by bicycles, horses, guns, wagons and trains)	3 per cent

Hospitalization.—The average period of hospitalization in 100 consecutive cases was twenty-seven and twenty-four hundredths days per patient. These stays ranged from one to one hundred and thirty-two days.

Mortality.—There were 23 deaths recorded for the 398 cases. Fourteen patients died shortly after entry into the hospital (minutes to twelve hours), and all had multiple injuries and were simply given local surgical first aid plus the usual shock therapy. Two of the remaining deaths were caused by delirium tremens and 3 by pneumonia; 1 patient died after a cerebral hemorrhage thirty-six hours after entry, and 1 died of embolism four days after entry. Two died after primary amputation,

both with multiple injuries, and 1 died after a secondary amputation for gas bacillus infection forty-eight hours after entry. (The last-mentioned patient had a massive, dirty compound fracture of the lower part of the left leg, involving the knee; the "first aid" treatment consisted in application of a dirty rope tourniquet and a manure-soiled plank for a splint, and the patient was brought to the hospital on the floor of a taxicab!)

Sepsis.—Sepsis occurred in 28 cases. This ranged from mild local wound infection to virulent sepsis and osteomyelitis. Five of the patients reported to the hospital from twelve to thirty hours after injury and were already infected or practically so. The other 23 patients showed the following types of sepsis: Sixteen had local wound infections which cleared up in periods ranging from one to four weeks; three had local osteomyelitis (in 1 case a thumb with a compound fracture caused by the bite of a vicious dog had to be amputated), and 3 had gas bacillus infection (2 of these came to amputation, and the infection of the other cleared up under local and general therapy). It is also to be noted that of the 23 wounds 4 were initially left open and treated by the Orr method and 2 were left open and dakinized (treated with diluted solution of sodium hypochlorite U. S. P.); the remainder were given primary suturing.

Properly, the treatment of the compound fractures observed over this five year period should have begun at the scene of the accident. Unfortunately, the first aid treatment in these cases was for the most part crude and did more harm than good. However, this situation is, I sincerely hope, now corrected, owing to the dogged perseverance and work of Dr. William Reggio in connection with the local police department.

TREATMENT

Initial Measures.—Treatment of compound fractures in this hospital, as has been mentioned, begins on the accident floor. There an examination is made of the patient as a whole by one physician while the compound injury and the patient are given initial treatment. Because of the terrific smash injuries by automobiles today, the general examination must be carefully carried out. The examiner has to bear in mind all sorts of complications. Besides shock and hemorrhage, he must look for injuries to the skull, the spine, the chest, the kidneys and the abdominal viscera and many other things. The large number of cases of multiple trauma makes this paramount today.

The initial treatment consists in immediate institution of shock and hemorrhage therapy (heaters, blankets, morphine), exposure of the compound fracture and its immediate covering with a sterile dressing.

Then come removal of all clothing and temporary traction and fixation of the fracture by a Murray-Jones arm splint, a Keller-Blake leg splint or a "pillow and sides" splint, as the condition requires. After this preliminary examination and treatment, if the patient's condition is satisfactory, a roentgen examination is made, and the patient is then taken to the operating room.

If, however, the patient is in severe shock on arrival, he is at once transported to a shock room, where he is put into a shock bed equipped with blankets and electric pads. He is given morphine, his clothing is removed, the wound is dressed and the fracture is temporarily splinted. (As much as possible of this is done under blankets.) Treatment of the shock is then continued along the lines suggested by one of the staff members, Dr. Kenneth Coonse. At this hospital my associates and I still have to depend on the not too accurate method of gaging traumatic or hemorrhagic shock by the systolic and diastolic blood pressure. Any pressure below 90 is potentially dangerous, and any pressure which persists below 80 is insufficient for adequate circulation in the peripheral tissues. As Coonse has stated, it is important in cases of surgical shock to institute prompt treatment sufficient to restore an adequate level of blood pressure, together with adequate red corpuscles and serum proteins. This, of course, is best accomplished in the majority of cases by transfusion of whole blood. In cases of severe shock, restoration of the blood volume is the first and most important procedure. As no "blood banking" system has been established at our hospital, a definite interval elapses between the patient's arrival at the hospital and the actual transfusion. This time is valuable, and so while waiting for the typing and the donor we make use of a special sodium bicarbonate solution in combination with hypertonic dextrose or saline solution, as directed by Coonse. This sodium bicarbonate solution is of about 7 per cent strength and comes in 50 cc. ampules. It is given if necessary at half-hour intervals until the transfusion is actually being given. The blood is given generally in citrated form (though some still give whole blood by the Kimpton tube method) and amounts to about 500 cc. As a rule the patient responds rapidly to this intravenous sodium bicarbonate treatment and in the majority of cases can be taken to the operating room via the x-ray room within an hour of arrival at the hospital. This fact, I believe, has aided greatly in lowering the incidence of sepsis.

In all cases, after testing and desensitization a prophylactic dose of 100 cc. of gas gangrene antitoxin and 1,500 units of antitetanus serum are given intramuscularly. Patients having large macerated wounds or extremely dirty ones are given the same amount of gas gangrene antitoxin with 5,000 units of antitetanus serum, and this dose is repeated twice during the first ten days.

Anesthesia.—The type of anesthesia is selected by the surgeon and the anesthetist after a check-up of the patient's local and general condition. The types of anesthetic used are spinal anesthetic agents, nitrogen monoxide and ether, nitrogen monoxide and oxygen, avertin in amylene hydrate with ether, intravenous pentothal sodium with or without a local anesthetic and, occasionally, local anesthetics. Cyclopropane is also given when indicated.

Preparation of the Wounded Area.—As soon as full anesthesia has been attained, an assistant removes the temporary splint, maintaining traction, while a second carefully shaves the limb about the wounded area. If the skin is covered with oil or grease, a careful preliminary cleansing with benzine or ether is done by the second assistant. This cleaning is all done with the wound carefully covered with sterile gauze, which has replaced the initial dressing after material for a "wound culture" has been taken.

With this sterile dressing carefully held on the wound, an assistant who is scrubbed and is wearing sterile gloves begins a thorough centrifugal cleansing of the skin surrounding the wound with soap and water. The cleansing is done by sterile gauze pads, and at least fifteen minutes is consumed in this. The skin is then carefully wiped with gauze soaked in saline solution followed by ether.

This assistant now changes his gloves, removes the sterile pad from the wound and replaces it with one that just fits the wound itself and not the edges. The edges are then given a cleansing with soap and water followed by ether. Again the assistant changes his gloves, soap and water, removes the pad from the wound and proceeds to clean the wound itself with sterile gauze and water and soap, following this with an ether wash.

Débridement.—The surgeon steps in and drapes the wound in the usual manner after wiping the skin and then the wound with ether or alcohol or, sometimes, painting it with a 2 per cent iodine solution. He then proceeds to excise the traumatized lacerated edges of the wound, generally to a width of not more than ⅛ inch (0.32 cm.). This is done cleanly with a forceps and a knife. Extreme care must be taken not to excise too much of the edge of the skin. The operator then changes instruments and commences the débridement proper. During this, gentle irrigation with warm salt solution is going on. No forceful stream is used.

In regard to débridement proper, the technic described by Wilson and Cochrane [2] is, with some exceptions, essentially followed.

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2. Wilson, P. D., and Cochrane, W. A.: Fractures and Dislocations, Philadelphia, J. B. Lippincott Company, 1925, pp. 49-57.

General Details of Technic: For the operation itself, the most careful technic is required. The surgeon should employ instruments altogether in handling of tissues and avoid putting the gloved finger into the wound. A frequent change of soiled instruments for fresh sterilized ones is necessary, and if the gloves become contaminated from the wound, they should be immediately changed, or carefully washed in strong antiseptic solution. Great pains must be taken to avoid traumatization of healthy tissues by seizing them roughly with forceps.

Retractors should be used gently. Sponge by pressure rather than by wiping, as the latter spreads infection into sterile parts. Careful hemostasis must be obtained, as blood clots favor the growth of bacteria. Avoid ligation en masse, as the tissue tied off is deprived of blood supply and furnishes excellent media for organisms. Deep sutures and ligatures should be made with fine catgut and the knots cut short. Suture and ligature material constitute foreign bodies and favor the development of infection.

The operation is best performed by the method of progressive excision of the walls of the wound. When possible this may be done by block removal to a considerable extent, but it is never possible to deal with the entire wound in this manner, and the danger is always in the excision of too much tissue. The surgeon should be especially warned against this fault, as it is one that has frequently brought the operation into disrepute.

Excision of Damaged and Infected Tissues: The external wound opening should be excised with a surrounding strip of skin 7 mm. to 1.25 cm. wide. Complete access to the wound should then be obtained by an appropriate incision. The subcutaneous tissue, being less important, may be removed more widely. The walls of the wound where they are distinct may be excised en bloc. When this is not possible, the surfaces should be carefully inspected, and damaged and soiled tissue removed whenever found. When the blood supply is good, as indicated by free bleeding, it is sufficient to remove a layer 6 mm. thick. If, however, the normal oozing is absent, the tissue should be excised. Blood clots should be removed and bloody infiltrations traced back along the fascial planes. Lacerated tendon sheaths should be opened and the tendons, depending on their condition, either removed or thoroughly cleansed.

Treatment of Muscle Tissue: Muscle tissue should be treated with great care. It should never be sectioned transversely beyond the part which needs to be removed, as it does not regenerate and there is also likely to be injury of the minute nerve fibers running within the muscle itself. However, it is the favorite site for the development of gas infection, and all damaged and soiled tissue must be thoroughly removed. Healthy muscle may be recognized by its normal color, the oozing of minute drops on section, and its contractible response on stimulation with forceps.

In a modified way this technic has been followed by my associates and me. It must be emphasized that excision en bloc requires extremely good surgical judgment. It would probably be safer to recommend generally a careful, systematic removal of devitalized tissue wherever found. It is only the occasional fresh compound fracture that we enlarge by incision into neighboring tissue. It is our belief that the procedure is unnecessary in most cases and only adds more trauma, opening fresh tissue and thereby increasing the possible incidence of sepsis. It should be limited to the few instances in which internal fixation is needed, where there is considerable underlying traumatized and devitalized tissue,

or in which a simple plastic operation is to be done. Again, though we remove blood clots, we believe in not disturbing the fascial planes to any considerable extent in tracing bloody infiltrations. Also, we are ultraconservative in dealing with tendon sheaths and tendons.

Irrigation.—After the débridement the wound is thoroughly but gently irrigated with warm salt solution followed by an ether wash, care being taken to avoid the bone and its coverings in performing the latter.

Treatment of the Fracture Proper.—The surgeon now again changes his gown and gloves and redrapes the operating field. With an entire fresh set of instruments he treats the fracture proper. The fractured ends are gently curetted to remove all possible contamination; the instrument is discarded, and the wound is again gently irrigated. If the fracture is comminuted, extreme care is exercised in compact handling of the fragments. At this stage we bear in mind what Rutherford [3] said in regard to this: "The leaving of bone fragments in a comminuted fracture is the surest way of securing natural and rapid repair, while the removal of these fragments is the surest way of securing ununited fracture."

We agree with him that it is extremely rare for a piece of bone in the ordinary compound comminuted fracture to be severed from all vascular supply. A piece of bone may be separated from the main shaft but not from the organically connected soft parts. Therefore, loose and comminuted fragments of bone should not be removed unless they are practically extruded from the wound and completely separated from all blood supply.

Choice of Procedure.—From this point forward the treatment will proceed according to the surgeon's experience and judgment.[4] I realize that some surgeons will proceed exclusively along conservative lines; that is, they will never plate, band, suture or nail this type of fracture. My associates and I unhesitatingly do so if we think the fracture requires it and if in our judgment the patient's condition warrants it.

Roentgen examination plays its part at this stage and often determines the decision between internal fixation and conservative treatment. Because of improved methods of enclosed fracture treatment it is found that only a small percentage of these fractures require internal fixation. But, as I have said, when a compound fracture needs internal fixation and the patient's general condition is good, we use it. Because of the relatively high incidence of delayed union and nonunion in these frac-

3. Rutherford, A. G.: Management of Fractures of the Femoral Shaft, West Virginia M. J. **22**:6, 1926.

4. Forrester, C. R. G.: Imperative Traumatic Surgery, New York, Paul B. Hoeber, Inc., 1929, chap. 18.

tures, accurate reduction and apposition are paramount. Internal fixation is sorely needed in some cases. In the selected instances in which my associates and I have felt the need of internal fixation and use it, we have found the wound remaining free from sepsis and giving relatively early good end results. Such results have shown us that the addition of the trauma of internal fixation to that of the original injury does not necessarily mean later sepsis. The use of such foreign materials as plates, screws and wires is not contraindicated because of their instigating later sepsis. Also, internal fixation has the advantage of absolute holding of the snug approximation, resulting in earlier union; it gives relief from pain; it prevents spread of infection, and it permits ease of handling of the patient, an all-important factor from the nursing and the convalescent standpoint. These arguments again uphold the contention that a great deal of judgment and experience is necessary before the surgeon can determine accurately the best method of treatment in each case.

The next stage of compound fracture therapy is controversial. Shall the wound be left open? Shall it be treated by the Orr method, by dakinization (irrigation with diluted solution of sodium hypochlorite U. S. P.), by primary suture and temporary direct or dependent drainage or by simple primary suture?[5] I have neither space nor time to go into the arguments for and against these methods. Each has its many ardent advocates. I believe that they are all good methods. I feel that the surgeon should use that method which in his hands, in his experience and in his surroundings has been kindest to him and his patients. However, he should not be absolutely dogmatic in regard to its use. Cases will be observed in which there can be no doubt of the superiority of one of these methods, and then it should be used.[6] My associates and I happen to prefer as first choice the primary closure procedure without drainage. We have used it in roughly 85 per cent of our cases and the Orr method and dakinization in the remainder.

In compound fractures treated by the closed method the wound is closed in such a manner as to allow good tissue drainage; that is, no snug and sealed tight closure is attempted. These fractures are not drained by tube or by rubber dam. We depend entirely on our wide-spaced type of suturing for tissue drainage. With this closed method we make certain that the exposed area of bone is covered. If we find that the edges of the wound can be brought together only by great tension or not at all, we do not hesitate to promote closure by making

5. Graves, G. Y.: Primary Suture of Compound Fractures: Review of Seventy Cases, Am. J. Surg. **13**:539, 1931.

6. Scudder, C. L.: The Treatment of Fractures, Philadelphia, W. B. Saunders Company, 1926. Cotton, F. J.: Treatment of Compound Injuries, Surg., Gynec. & Obst. **52**:371, 1931.

lateral incisions on each side of the wound to allow the edges to be drawn together without tension. In cases in which this procedure is not sufficient a simple plastic operation is done. Above all, the wound should not be closed under tension, and there should be no exposed bone.

The open method is generally chosen by us when a good-sized area is involved; when there is considerable avulsion of tissue; when a considerable amount of dirt has been drawn into the wound, or when the patient has been in great shock and eight or more hours has elapsed since the accident. In such cases the fracture is treated finally by the Carrell-Dakin method or by the Orr petrolatum pack method. Later, when a smear shows a sterile field, a secondary repair of the fracture and the tissue is done.

Fixation.—The final step in the initial treatment for compound fracture, after the appropriate dressing has been applied, is the application of fixation. Patients in whom internal fixation has been established need, as a rule, only some simple type of external fixation, such as a plaster of paris cast with an appropriate and well placed "window." Some may be held in a well fitting arm or leg Thomas splint or even the old-fashioned Buck apparatus. A large percentage of those who have been treated conservatively (i. e., without internal fixation) and in whom the fracture has been more or less easily reduced do well with the molded plaster of paris cast with "windows" over the wounded area. Fractures with a marked degree of overriding or comminution with displacement are put up in traction in a Thomas arm or leg splint, a Thomas leg splint with a Pearson flexion attachment, a Jones humeral extension splint or the simple "crotch" humeral extension splint. Patients treated with the Thomas splint are generally put in suspension traction on the Balkan frame or on a goose-neck abduction frame. The types of traction used are: skin, Sinclair skate and skeletal (by Kirschner wire). I wish to warn against dogmatism as to the method used.

Unusual Fractures.—There is one type of compound fracture which differs from the usual (frank) kind. It is the pinhole, or puncture, type. Surgeons are not unanimously agreed on the treatment of this type of fracture. It is said that about 75 per cent of such wounds heal immediately, but, even granting this to be true, the surgeon who is confronted with an open fracture of this type can never be absolutely sure that it is not infected. The best basis for the treatment of such fractures is the assumption that they are all potentially infected. This is so whether the fracture is compounded from within or from without. All who have seen a number of compound fractures can recall tragic stories following a simple dabbing with iodine of the pinhole type of

compound fracture. My associates and I have decided that all such fractures should be treated by the regular excision-débridement method.

Again, there are a few cases of compound fractures in which the structures are so mangled and bones, muscles, vessels and nerves have been so obviously torn beyond repair that amputation is the only surgical solution. These are the obvious cases. There is a type, however, with which one too often lets an enthusiastic desire to save a limb overcome good surgical judgment. In such cases one forgets the inevitable later virulent sepsis or the slow or nonestablished collateral circulation causing gangrene and infection, and one amputates too late. This is not a plea for amputation as such. It is a plea to the operating surgeon to counsel wisely with himself and others in such borderline cases. He should and must remember the possible saving of life by primary amputation versus the temporary saving of the limb with a later inevitable amputation and probable loss of life from sepsis.

Complications.—Despite the conscientious and meticulous care given to compound fractures, the common enemy, sepsis, does appear and do damage in minor and major degrees. Its therapy, therefore, must be given due consideration. In some of our cases during the past two years we have been giving sulfanilamide as a prophylactic medicament to those patients in whose cases the initial culture showed some growth of streptococci. The two less frequent but virulent and deadly types of sepsis are the gas bacillus infection and tetanus. At the first sign of "gas" infection (the characteristic odor, loss of contractibility of the muscles when they are pinched with a forceps and their discoloration, pain, elevated temperature and pulse rate, crepitus, a tympanic area about the wound or the beginning of cutaneous mottling) specific treatment should be instituted at once.

The original culture of material taken from the wound before its cleansing and débridement may give even earlier warning.

My rules for the treatment of gas bacillus infection are as follows:

1. Operate as soon as the diagnosis is made.
2. Make the local preoperative preparation as rapidly as possible, avoiding all unnecessary trauma.
3. Do not use tourniquets.
4. Make long, deep incisions.
5. Go between rather than through normal muscle fibers.
6. Excise all tissue which appears infected.
7. Sterilize the wounds as rapidly as possible with alcohol.
8. Place Dakin tubes into the wound in advantageous places, and pack gauze strips saturated in hydrogen peroxide about them.
9. Over all put sterile petrolatum gauze packs.
10. Connect Dakin tubes to a common tube through which fresh diluted solution of sodium hypochlorite U. S. P. (Dakin's solution) and

hydrogen peroxide can be injected alternately and which can be connected to an oxygen tank via a water bottle, so that between the irrigations with the sodium hypochlorite solution a fresh supply of oxygen is being constantly sent to the tissues.

11. Use 100 cc. doses of the specific anti-gas-bacillus serum daily or if deemed necessary at six hour intervals.

12. Stimulate with care.

13. Give frequent fractional blood transfusions.

14. Record the pulse and temperature every half-hour.

15. At the least sign of rapid spreading of infection or of increasing pulse rate and temperature, do a rapid guillotine or transfixion amputation and follow it with careful stimulation.

16. Perform the enumerated steps as rapidly as you can.

Tetanus, at least in this geographic area, is a rare complication today. However, when tetanus does appear we institute specific treatment at once. Our therapy follows along the general lines as laid down today. First, a careful intradermal test with the serum is given. If the result is positive, a most careful desensitization is done. One hour after this, an intravenous injection of 10,000 to 20,000 units is given subcutaneously and repeated at eight to twenty-four hour intervals until 200,000 units has been given. After this, an intravenous injection of 50,000 units is given. Twelve hours later the procedure is repeated. Today it is thought that massive doses should be administered as early as possible; not less than 100,000 units is advocated as an initial dose for all adult patients in whom the infection is not obviously mild. Even if symptomatic improvement occurs after large initial doses, the patient is given repeated doses of 50,000 to 100,000 units. It cannot be definitely concluded that intraspinal administration offers any advantage. It has also been found that dextrose (in vitro) is capable of neutralizing the tetanus toxin to a certain extent, and so in addition to the antitetanus serum, a daily 200 cc. intravenous injection of 10 per cent dextrose is given. The wound is, of course, left wide open and treated hourly with hot dressings wet with diluted solution of sodium hypochlorite or through Dakin tubes by alternating hourly irrigations with the sodium hypochlorite solution and with hydrogen peroxide. In conjunction with this the patient is transferred to an isolated, darkened room. Everything movable that is not needed in the room is removed. The door must have rubber checks. The nurses must wear rubber-soled shoes. Morphine, allonal (allylisopropylbarbituric acid with aminopyrine) amytal or avertin with amylene hydrate must be used to keep the patient quiet. For convulsive seizures a general anesthetic may be used.

The virulent Streptococcus haemolyticus infection also gives us considerable worry and work. We give the patient subpectoral and intra-

venous injections of physiologic solution of sodium chloride and dextrose solution. In some cases we give whisky or brandy. Sulfanilamide or one of its newer derivatives is also given routinely in these cases. We also see that a well chosen diet is given. However, the most important therapy for this virulent type of infection is repeated fractional blood transfusions. We are firmly convinced that such transfusions, judiciously dosed and spaced, have saved many patients. These transfusions may range from 150 to 500 cc. and can be of the citrated or of the whole blood type. A frequent check-up of the blood serves as a guide in regard to the frequency and time of the transfusions.

This treatment we give also for the serious Staphylococcus aureus infections. With all such infections we find that painstaking and alert special nursing is absolutely necessary for a happy outcome. Also, in cases of serious infection we confer with the internist in regard to the type of treatment. Our local treatment consists of adequate free drainage with active dakinization or frequent changing of hot moist dressings saturated with diluted solution of sodium hypochlorite, with hot flaxseed dressings over all. When extremities are involved, we make use of a specially wired bed cradle which is provided with electric bulbs to maintain an equitable warm temperature. We also make use of physical therapy; i. e., we give radiant heat by means of the infra-red lamp and also expose the patient locally and generally to ultraviolet rays. We usually put the patient into a suspension apparatus.

Despite this local radical surgical treatment giving adequate free tissue drainage, we have found that there is a certain type of compound fracture which is associated with a protracted elevation of temperature and a characteristic persistent pain. Fortunately such fractures are uncommon. The following case illustrates well the type to which I refer.

REPORT OF A CASE

In the spring of 1925 a girl 6 years of age was transferred to the Boston City Hospital from another hospital. Three weeks earlier she had sustained a most severe compound fracture of both bones of the lower part of the leg. She had been carefully and intelligently treated. The fracture had been treated from the beginning by the "open" method. It was well dakinized with diluted solution of sodium hypochlorite. Despite the careful treatment, sepsis crept in, and during the third week it was at its height. On two occasions well planned incisions and drainage operations were performed, yet the fever, the heightened pulse rate and the pain persisted. It was at this stage that she was transferred to the Boston City Hospital. The previous drainage of the soft parts was obviously adequate; so infection of the bone was the only possible cause of local pain. Therefore, the fractured ends of the bones were guttered and pus was found. Because of overriding, the ends were separated and held in Smith clamps in the reduced position. The wound was dakinized.

The child had immediate relief from pain after this operation. In fact, she had a remarkably smooth, uneventful convalescence. There was no marked seques-

tration. In six weeks, with good callus formation present, the Smith clamp was removed; in another six weeks the wound was clean and healed. The fracture was in excellent position and well united. Today the patient is about 21 years of age, and her injured leg is as long and straight as the other one and functions perfectly.

Cases like this showed us that compound fractures associated with persistent fever and pain despite apparently good tissue drainage need adequate bone drainage. I may also say here that, although we are not so enthusiastic as Baer was about his maggot therapy for acute uncomplicated osteomyelitis, I can truthfully say that for cleaning up obstinate, chronically septic compound fractures with the complicating osteomyelitis the Baer maggot therapy has proved very satisfactory to us.

Delayed Union and Nonunion.—There are two other annoying complications, and they are of great importance, especially economically. These are delayed union and nonunion. It is the general rule that compound fractures unite slowly and occasionally not at all. Because of this, one must give most of the patients specific medicine and diet (cod liver oil, viosterol in oil and so forth), as well as physical therapy (diathermy, ultraviolet irradiation, massage). Selected patients are given indirect stimulation by weight bearing with fitted ambulatory splints or properly prepared plaster of paris casts with Boehler walking irons or plaster soles and heels.

However, despite all this local and general specific treatment, there are occasional cases of obstinately delayed union in which the bone apparently will take many months to unite or to go to an ultimate state of nonunion. From our actual experiences with such cases my associates and I have come to the conclusion that the patients can be saved economically valuable months by some simple, stimulating bone-forming operation, such as the modern adaptation of Dr. Daniel Brainerd's hole drilling or that procedure plus an inlay graft, chip grafts or an osteoperiosteal graft. The great saving of time to the patient, insuring him a return to normal work and wages so much earlier, is a vital economic argument for this procedure.

SUMMARY

Intelligent first aid should be given in cases of compound fractures. This includes proper handling, modern emergency splinting and careful transportation.

In cases of compound fracture it is absolutely imperative to consider first, the patient and, second, the fracture. One should be prompt in giving proper rest, stimulation, prophylactic injections of anti-gas-gangrene and antitetanus serum and general supportive treatment with

an emergency dry sterile dressing and external traction and splinting. One should also be careful in the general examination to look for signs and symptoms of internal damage.

To insure good teamwork it is necessary to have well planned methods of preparation of the skin, débridement and cleansing of the wound. In treatment of the fracture itself, it is urged that surgeons be open minded. One should "size up" the situation quickly and be ready to use any of the several universally accepted methods for traction, internal fixation and other therapeutic measures.

One should not be dogmatic about "closed" and "open" wounds. One should be ready to use either the closed or the open technic according to one's judgment.

The type of external fixation should be chosen carefully.

One should counsel wisely and with others as to the question of primary amputation versus probable later amputation for complicating virulent sepsis with its probable fatal result.

In the treatment of later complicating gas bacillus or tetanus infection, one should give prompt and radical treatment with appropriate stimulation and supportive medical measures. The same may be said of the virulent streptococcic and staphylococcic infections.

One should consider bone grafting as a valuable time saver in carefully chosen cases of delayed union.

HIGH CHROMIUM, LOW NICKEL STEEL IN THE OPERATIVE FIXATION OF FRACTURES

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The purpose of this paper is to report the experimental and clinical use of high chromium, low nickel steel in the operative treatment of fractures in the service of Drs. William Darrach and Clay Ray Murray. The reason for the choice of this material derives from some of the difficulties encountered in the use of other metals as well as from the guiding work of Zierold,[1] who studied the interaction between a series of metals and living tissue, and of Jones and Lieberman,[2] who concluded that a high chromium, low nickel alloy is least objectionable for internal fixation.

Aside from the cases in which for mechanical or other reasons the operative method of treatment of fractures has failed, there has accumulated in this and other clinics a group of cases in which the plate or screws used in the mechanical fixation of the fractured bone have broken. The breaking of a vanadium plate or screws in such instances is a failure in treatment and sometimes a surgical tragedy.

In the face of these difficulties it is not easy to defend the operative treatment of fractures. However, a defect or a failure in method does not invalidate a principle, nor does a good principle justify a hopeless method. But because my associates and I believe that the operative method for the treatment of fractures is justified under controlled circumstances,[3] we seek to improve the method and reduce the hazard of accidental failure.

METALLURGIC CONSIDERATIONS

From extended clinical experience it became obvious that the vanadium alloy failed in certain respects. There are many cases in which it is necessary to remove the metal used for fixation because

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1. Zierold, A. A.: Reaction of Bone to Various Metals, Arch. Surg. **9**:365 (Sept.) 1924.

2. Jones, L., and Lieberman, B. A.: Interaction of Bone and Various Metals: Vanadium and Rustless Steel, Arch. Surg. **32**:990 (June) 1936.

3. Murray, C. R.: Primary Operative Reduction of Fractures of Long Bones as a Method of Choice: An Evaluation of Principles, read before the Section on Orthopedic Surgery of the American Medical Association, St. Louis, May 19, 1939; to be published.

of evidence of local irritation, pain and absorption of bone around the metal. At removal there are corrosion of the plate or screws, unhealthy tissue granulation and even exudate, which, when examined by the usual bacteriologic methods, proves to be sterile. This is apart from the cases in which there is failure of internal fixation or of the plates or screws. In fact, susceptibility to corrosion has been used to explain the breaking of the metal.

Nor is this all. Those who champion the operative method have had to deal as well with an old prejudice—a prejudice which may have considerable foundation but which, with the use of better methods, surgeons may outgrow. In this service it is considered good surgery to place foreign bodies in tissue or even in compound wounds if it contributes to fixation of fractures and therefore reduces spread of infection (Darrach [4]). However, this departure from an accepted method is not easy to defend. Experience shows that vanadium alloy is frequently unable to withstand the oxidizing, reducing and electrolytic [5] influence of tissue juices. Particularly is this true in cases of compound fractures which have gone on to infection. However, infection is not the important factor, because absorption of bone and the other changes previously mentioned can take place in a perfectly clean wound.

The blame for its shortcomings cannot be placed on the vanadium alloy. An important factor has been that, though the preparation is standardized, the quality of the plates put on the market cannot be controlled. This was proved conclusively when plates of various origins were tested for resistance to minute vibratory stresses not surpassing the elastic limits of the steel.[6] Many plates subjected to 3,000,000 to 5,000,000 vibrations appeared in crude test to be just as tough afterward as before, whereas others became so brittle that they could be snapped by hand. This was not true of the high chromium, low nickel alloy plates similarly tested. In fact, they seemed less ductile but tougher (i. e., to crude twisting and bending deformations) and yet not brittle.

These defects have been investigated by others, and some of the causes have been attributed by Martin [7] to several sources.

The failure of bone plates and screws can be traced to methods of manufacture that are not in compliance with the Commercial Standards CS37-31, Bureau of Standards, U. S. Department of Commerce. The methods employed are such

4. Darrach, W.: Treatment of Compound Fractures, Surg., Gynec. & Obst. **66**:815, 1938.

5. Venable, C. S.; Stuck, W. G., and Beach, A.: The Effects on Bone of the Presence of Metals, Based on Electrolysis, Ann. Surg. **105**:917, 1937.

6. Fulton, J. F.: Muscular Contractions and Reflex Control Movement, Baltimore, Williams & Wilkins Company, 1926.

7. Martin, D. J.: Personal communication to the author.

that both the bone plates and the screws were of unsound design from an engineering point of view. Sharp corners at the bottom of the screw holes in the various plates provided sections subject to enormous stress concentration, from which failure invariably started. Excessive depths of the centering holes in the screw heads produced sections of extreme weakness when the centering holes entered the threaded sections of the screws. Failure of screws occurred in these sections.

In addition to the mechanical faults noted above it is felt that the hardness and chemical composition set forth in CS37-31 are not the most desirable for the purpose. . . . It would seem that certainly a softer material, and, perhaps, even one of different chemical composition, would better serve the purpose of these parts.

Cases have been observed in this clinic in which the vanadium steel plate was broken postoperatively and after bony union had taken place. That is, the length of time during which the plate was in the body did not seem to be a decisive factor. In other words, it may be doubted that the break took place as a result of prolonged electrolytic corrosion or, on the other hand, because of fatigue failure. The most likely explanation involves both factors and adds that the plates were essentially defective as a result of the manufacturing process. The following illustrative data were culled from the operative records.

Patient D. R.; fracture of the shaft of the tibia; broken plate discovered on the first postoperative day, while the fracture was in suspension.

Patient M. D.; fracture of the radius; broken plate discovered eight days after the operation, with the fracture in a "sugar-tong" splint.

Patient S. S.; compound fracture of the femoral shaft; broken plate discovered twenty days after the operation, with the fracture in suspension.

Patient M. S.; fracture of the femoral shaft; broken plate discovered twenty-two days after the operation, with the fracture in suspension.

Patient T. D.; fracture of the radius and ulna; broken plate discovered five weeks after the operation, with the fracture in a "sugar-tong" splint (plate used on the radius only).

Patient M. P.; fracture of the femur; broken plate discovered sixty-two days after the operation, while the patient was moving the leg in a brace.

Patient C. S.; fracture of the femur; broken plate discovered thirteen days after the operation, with the fracture in a tubular plaster splint.

REASONS FOR THE USE OF HIGH CHROMIUM, LOW NICKEL STEEL

In choice of materials for experimental and clinical use my associates and I were guided chiefly by the work of Zierold, who reported the adverse influence of certain metals, including nickel, on bone healing but cited the relatively inert nature of stellite. This work was extended by Jones and Lieberman, who considered not only the relation of the material to the tissues but that of the tissue juices to the material. Since that time, the advent of high chromium, low nickel steel on the com-

mercial market at a relatively low cost and the increase in knowledge of handling the material have recommended it for use. Unlike vanadium, the American product is easily available, and its composition and preparation are subject to careful control.

The material used was produced by the Crucible Steel Company of America and fell into the Rezistal KA2 and FM188 groups. These are trade designations for the austenitic group of alloys recommended [8] for their properties of resistance to corrosion.

Chemical Composition.—The composition of the alloy in percentage, according to a bulletin of the Crucible Steel Company, is as follows:

Chromium	17-19
Nickel	8-9.5
Carbon	0.7 maximum
Phosphorus	0.1 maximum
Sulfur	0.15 maximum
Molybdenum and selenium	optional

Physical Properties.—As reported in the Crucible Steel Company's catalog, some of the physical properties of the alloy are:

Tensile strength	85,000 to 95,000
Yield point	30,000 to 40,000
Elongation in 2"	55 to 60%
Reduction of area	65 to 75%
Brinell	130 to 170
Charpy	100
Thermal conductivity (gram calories per cubic centimeter, per second, per degree Centigrade)	0.052
Specific gravity	7.94
Specific heat	0.118
Melting point (deg. F.)	2,550

Specific electrical resistance (microhms per cubic centimeter)

20 deg. C.	73
100 deg. C.	90
500 deg. C.	106
800 deg. C.	111

Coefficient of linear expansion (per degree Centigrade)

0 to 100 C.	0.000016
0 to 600 C.	0.000018
0 to 1,000 C.	0.000020

Modulus of elasticity ..... 28,000,000 to 30,000,000

There are several conditions in the manufacture and finishing of the steel which have important bearing on its behavior. Cold working

8. Bergen, L. S.: Personal communication to the author.

markedly increases the "Brinell," or relative hardness, and makes the metal less ductile. This has also some relation to the contour of the grain and distinctly reduces resistance to corrosion. Cutting, drilling, milling and threading must be done with lapped tools with a smooth, sharp cutting edge and with adequate clearance to minimize the "tearing" which can occur in the soft state. The final surfacing of the steel is extremely important. It should be polished and buffed with a nonferrous material and afterward passivated by immersion in 20 per cent nitric acid at 65 C. for a half hour to give, theoretically, a molecular chromic oxide coating. Great care should be exercised to remove whatever fragments or microscopic grains of iron or steel may be left in the surface as a result of machining.

These processes are carried out to reduce to the minimum foci for electrolytic corrosion. If properly handled, the material should be practically noncorroding even in the presence of infection and electrolytically inert in tissue fluids. It should have a fair degree of ductility, which makes it possible to form it to the contour of the bone. Although its tensile strength is not so great as that of the vanadium alloy, it is adequate to the needs, and in experimental work and clinical surgical application by other members of the staff as well as by myself in 98 consecutive cases I have yet to discover failure because of the metal itself. In clinical use I have found that the presence of the steel, even in compound wounds in which the metal is exposed to the external atmosphere, does not inhibit osseous repair. In fact, if the devices (plates or screws) are not too superficially placed, granulation tissue will cover them, and it is possible to pinch graft regions of loss of soft parts and skin.

USE OF THE FIXATIVE APPARATUS

The scope of this paper does not cover the importance of organization of a fracture service [3] in the successful treatment of fractures and takes for granted the use of a meticulous nontouch surgical technic. But there are many details in the application of technic which bear directly on the effectiveness of a method.

The first condition for successful use of the operative method is adequate surgical exposure. It may be added that, although exposure is relatively simple in the superficial tibia and ulna, it is better to place the plate and screws deep in soft tissue rather than near the skin. In compound fractures it may be expedient to depart from this rule, but in such a departure secondary removal of the device used for internal fixation is frequently necessary.

With good exposure the second necessary condition may be more easily accomplished, i. e., anatomic reduction. This implies thorough

study of the roentgenograms before operation and familiarity with the use of bone-holding forceps. But reduction is not enough. That the third condition may be fulfilled, holding the reduction during fixation is a prime requisite. This must be done with a minimum of periosteal stripping. If the periosteum is stripped or extensively torn, it should be removed in part to eliminate it as a potential barrier to revascularization of the cortical bone.

The most important condition to be fulfilled is adequate rigid internal fixation. This is not always easy. The presence of multiple fragments may make internal fixation very difficult and sometimes impossible. However, in a usual case the following points should be borne in mind:

1. The plate must be formed to fit the contour of the bone by gentle use of small bending irons.
2. The plate should be held to make possible the accurate placement of drill holes, these being vertical to the long axis of the bone.
3. The drill used should be the size used in machine practice, the thread tap being fitted to the proper screw.
4. The hole must be bored with a sharp drill with good clearance and in true line to avoid reaming the hole and making it large for the cutting screw, thus producing a "sloppy" fit.
5. The self-tapping screw when driven must be in the exact line of the drill hole to engage the opposite cortex when that is sought.
6. When all the screws are in place, they should be "snugged up" firmly but not roughly to take out all play between the bone and the plate and plate and the screws. Stripping of the thread in the bone, however, should be avoided.
7. The screws must be so placed as to avoid injuring the thread against the plate.
8. The plate must be long enough to clear the fracture site and in proportion to the length of the fracture and of the bone.
9. It is of the utmost importance to place one or more separate oblique screws crossing the fracture and vertical to the screws fastening the plate to take up the torque stresses invariably present.
10. When possible, it is wise to engage both cortices. Particularly is this true in the presence of a deep-lying loose fragment.

TISSUE REACTION

Observations were made of the reaction of tissues to the material under discussion.

MATERIAL AND METHOD

Mature dogs were used for observation of the behavior of high chromium, low nickel steel in living tissue. It seemed unnecessary to repeat the work of Jones and Lieberman in the in vitro experiments. The use of screws not taking

any stress of function appeared too limited in application. Accordingly, small screws and plates were made and put into dogs just as in the clinical operative treatment of fractures. At operation one of the long bones to be plated was fractured with a chisel or a bone-cutting forceps or both. The fracture was reduced and fastened with four screw plates, such as are now used to repair small bones of the forearm or metacarpal bones. The screws were self tapping, with a sharp cutting edge (figs. 1 *B* and 6). A special screwdriver giving rigid control of the screw in rotation and long axis (fig. 1 *A*) and a modified nontouch technic were used throughout.

The plates and screws were fabricated (fig. 2) by the special methods employed for this type of metal. After fabrication they were carefully cleansed in soap

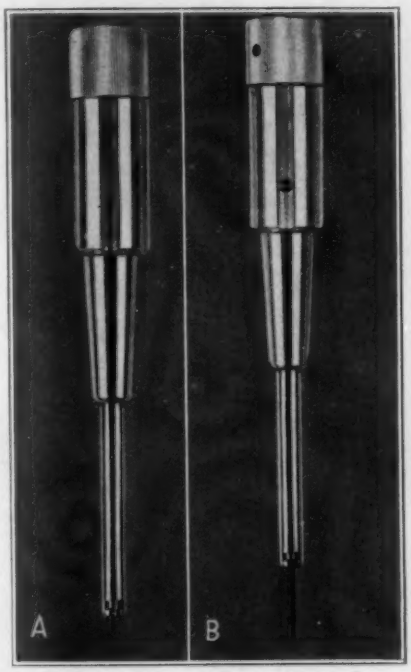

Fig. 1.—*A*, screw driver designed and perfected by Mr. Joseph Becker, of the department of pharmacology, College of Physicians and Surgeons, Columbia University, with a knurled head driven home and used as an ordinary driver. *B*, same driver with the screw in position and gripped.

and water, alcohol and ether. They were desiccated in an oven for twelve minutes to one-half hour at 112 C. and over calcium chloride for twenty-five minutes and were then weighed.

The animals were killed at different periods up to two years. The shortest period for which the metal remained in place was two days. This was in the first animal, which was operated on soon after arrival from out of town. It died postoperatively of bronchopneumonia.

PROTOCOL FOR AN ANIMAL KILLED AT TWO DAYS

Dog 1.—A brown and white pointer bitch weighing 15.2 Kg. was used. Osteotomy of the right radius was performed, with a plate and screws.

On Dec. 2, 1936, preparation was made with soap, water, alcohol, ether and iodine. The anterolateral approach was used. Towels were fastened to the skin with clips. Anesthesia (ether) was induced by the open method. The periosteum

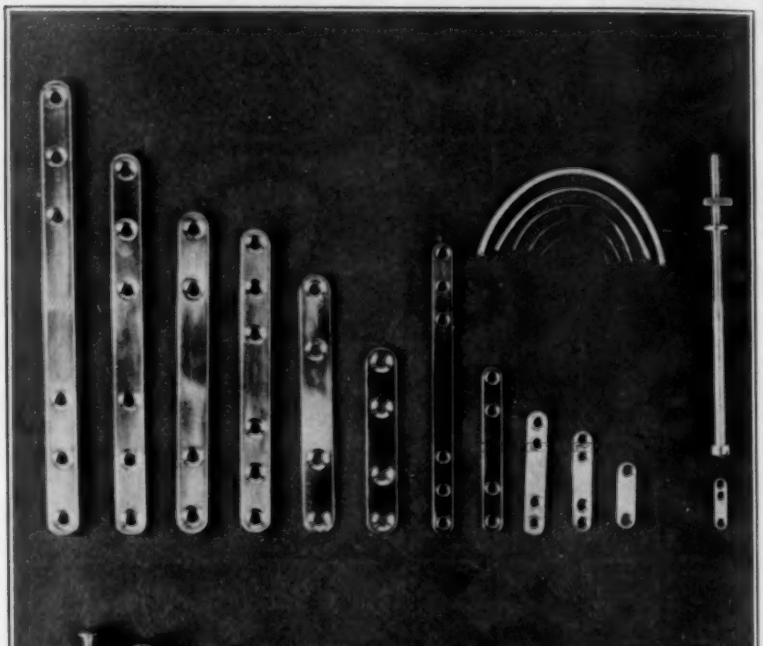

Fig. 2.—Plates, screws, bolt and wire routinely used in the operative fixation of fractures. This equipment is made and marketed by Mr. Joseph Becker, previously mentioned.

was stripped. The radius was broken with a flat osteotome. A no. 41 drill, a no. 10 plate and four screws (nos. 1, 9, 6 and 7) were used for fixation, which was rigid. The wound was closed in three layers.

On December 3 there was a good deal of edema. The breathing was labored and irregular. Early pneumonia was present. There was no tension on the sutures. The dog could touch the foot to the ground.

Fig. 3.—*A*, preoperative film of a compound fracture of the right tibia. *B*, another projection. *C*, roentgenogram taken on the first postoperative day, with the fracture in suspension. *D* and *E* show appearance nine months after operation.

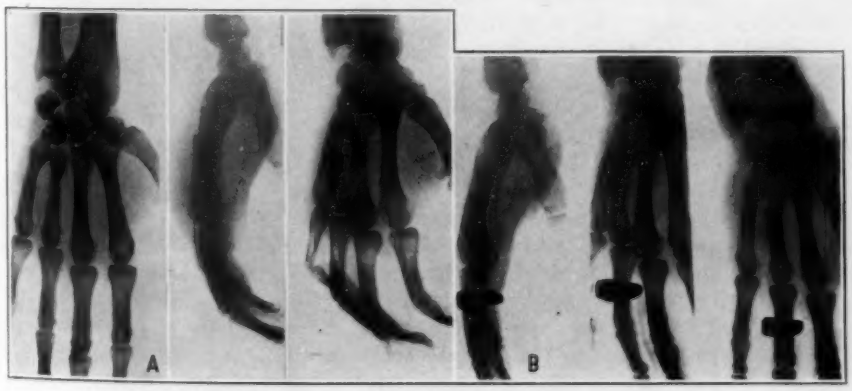

Fig. 4.—*A*, preoperative film, and *B*, film taken nine months after operation. The films illustrate the use of the metal in fractured metacarpal bones.

The animal died early in the morning of December 4. Extensive consolidation of the right lung and some consolidation of the upper lobe of the left were noted. There was a film of coagulum over the plate and screws in the right radius.

The following data were recorded:

No. 10 plate	1.1897 Gm. at operation
	1.1891 Gm. at removal
	0.0006 Gm. loss
	0.06 per cent loss
No. 1 screw	0.2903 Gm. at operation
	0.2895 Gm. at removal
	0.0008 Gm. loss
	0.2 per cent loss
No. 6 screw	0.4876 Gm. at operation
	0.4876 Gm. at removal
	0.0000 Gm. loss
	0.00 per cent loss
No. 7 screw	0.4556 Gm. at operation
	0.4554 Gm. at removal
	0.0002 Gm. loss
	0.004 per cent loss
No. 9 screw	0.2904 Gm. at operation
	0.2898 Gm. at removal
	0.0006 Gm. loss
	0.2 per cent loss

PROTOCOL ON AN ANIMAL KILLED AT FORTY-NINE DAYS

Dog 13.—A dark spotted hound weighing 16.5 Kg. was used. Osteotomy of the right radius was performed, with application of a plate and screws, on Dec. 16, 1936. The usual aseptic technic was employed. Ether anesthesia was induced by the open method. The anterolateral approach was used. Rigid fixation was obtained by means of a plate (no. 10) and four screws (nos. 1, 7, 6 and 9). These appliances were from a new batch.

On December 21 the leg bore weight. The dog was lively. There was some redness about the wound.

On Feb. 3, 1937, the dog ran well, with good use of the foot. Roentgenograms were taken, and the dog was killed. The proximal two screws were covered with dense fibrous tissue which separated easily from the plate. The distal part of the plate and the distal screws were almost completely covered with dense bone. In the groove of the head of the most distal screw (no. 9), bony tissue was present; all screws were removed with difficulty. The screws and plate appeared smooth and shining; there was no evidence of corrosion. The tissue about the plate was pinkish white. The fracture line was well healed and slightly paler than the tissue nearby.

The following data were recorded:

No. 10 plate	1.2154 Gm. at operation
	1.2143 Gm. at removal
	0.0011 Gm. loss
	0.08 per cent loss
No. 1 screw	0.2874 Gm. at operation
	0.2875 Gm. at removal
	0.0001 Gm. gain
	0.03 per cent gain
No. 6 screw	0.4695 Gm. at operation
	0.4697 Gm. at removal
	0.0002 Gm. gain
	0.04 per cent gain
No. 7 screw	0.4478 Gm. at operation
	Loss of weight in removal; not used
No. 9 screw	0.2768 Gm. at operation
	0.2771 Gm. at removal
	0.0003 Gm. loss
	0.1 per cent gain

PROTOCOL ON AN ANIMAL KILLED AT ONE HUNDRED AND NINETY-SIX DAYS

Dog 8.—A mixed "collie mongrel" bitch weighing 15.3 Kg. was used. Osteotomy of the right tibia was done, with application of a plate and screws, on Jan. 6, 1937. Soap, water, alcohol, ether and iodine were used in preparation. Ether anesthesia was induced by the open method. The anterolateral approach to the right tibia was used. Osteotomy was done at the junction of the upper and the middle third. The periosteum was stripped. The fracture was reduced and fixed with a plate (no. 10) and four screws (nos. 1, 7, 9 and 6).

On January 7 there was some edema of the leg and paw. There was a suggestive cough. The dog was friendly.

On January 8 the dog was in good spirits and ate well. More edema was observed. The wound was clean.

On July 21 the dog was killed. The no. 9 screw was removed with great difficulty. It was injured, with loss of weight. The no. 6 screw was so well healed in that the tip broke.

The following data were recorded:

No. 10 plate	2.5458 Gm. at operation
	2.5445 Gm. at removal
	0.0013 Gm. loss
	0.2 per cent loss

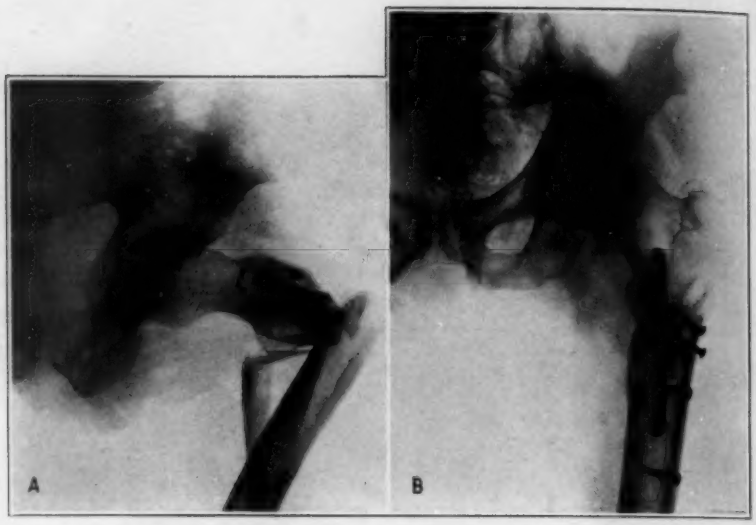

Fig. 5.—Complicated subtrochanteric fracture of the left femur, before operation (*A*) and after union had taken place (*B*).

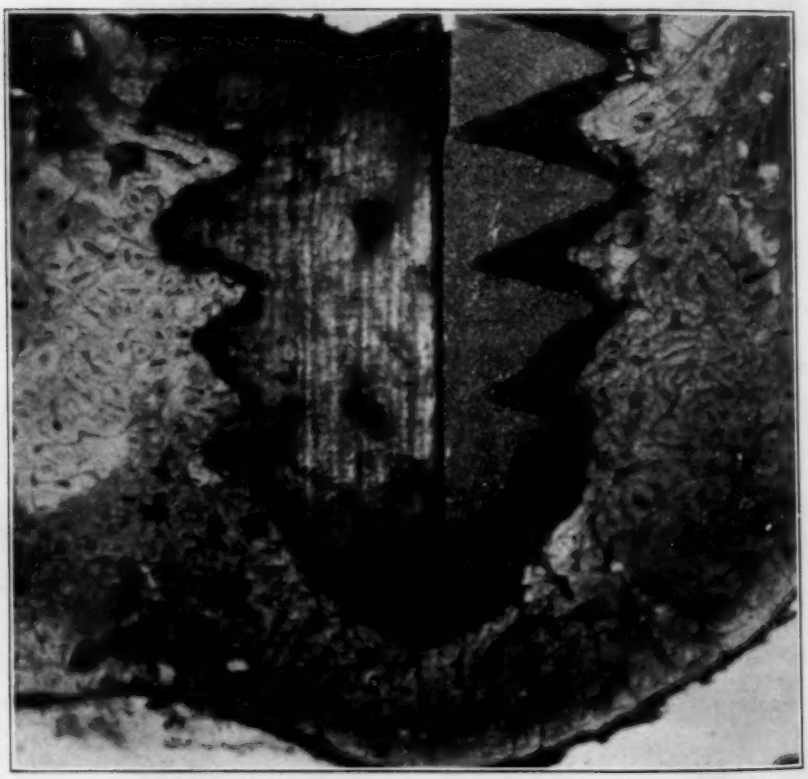

Fig. 6.—Section of the broken screw tip (no. 6 screw) in dog 8, killed at 196 days. The photograph is a magnification approximately 50 times of the screw tip embedded in bone tissue. Note that one half of the metal shows its granular surface; the other half is covered by bone substance, which has healed into the recess which bounds the sharp self-tapping threads. The photomicrograph was taken with combined transmitted and reflected light. Hematoxylin and eosin stain.

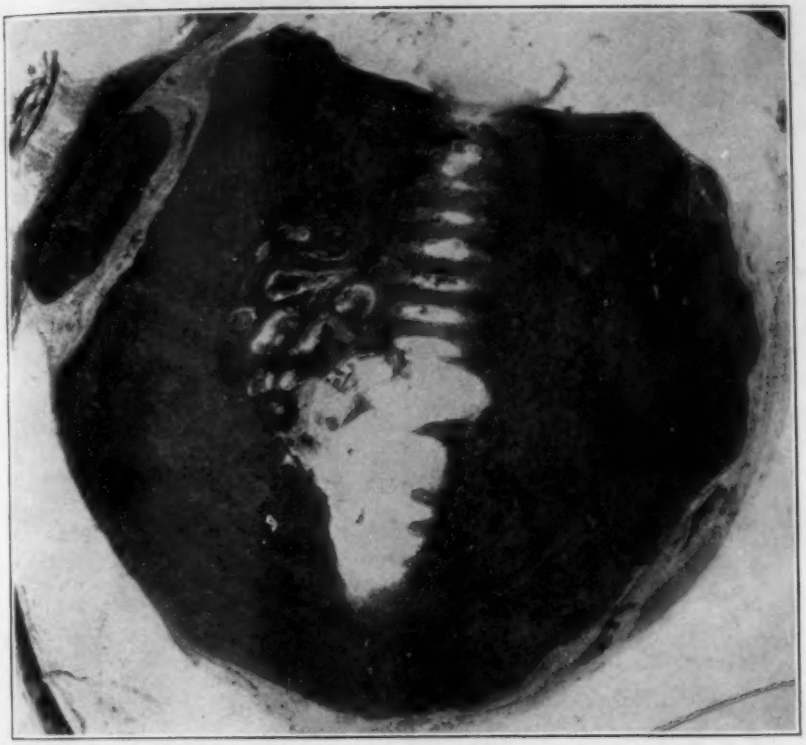

Fig. 7.—Another screw hole (same animal as in figure 6), showing the survival of bone tissue in the grooves of the screw threads. Approximate magnification, × 12. Hematoxylin and eosin stain.

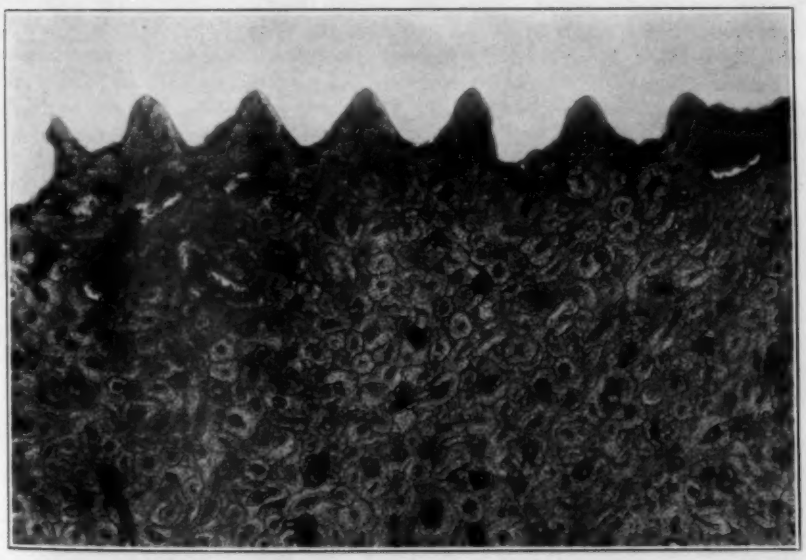

Fig. 8.—Section of a dog's radius in the long axis of the screw hole. Note the ridges which represent bone tissue of the thread approximating the screw. Approximate magnification, × 50. Hematoxylin and eosin stain.

No. 9 screw..... 0.4824 Gm. at operation
0.4807 Gm. at removal

0.0017 Gm. loss of weight; not not counted; screw injured
0.3 per cent loss of weight

No. 7 screw..... 0.4776 Gm. at operation
0.4771 Gm. at removal

0.0005 Gm. loss
0.1 per cent loss

No. 1 screw..... 0.4795 Gm. at operation
0.4792 Gm. at removal

0.0003 Gm. loss
0.06 per cent loss

No. 6 screw..... 0.4902 Gm. at operation; broken at removal; used for section

PROTOCOL ON AN ANIMAL KILLED AT THREE HUNDRED AND SIXTY-SIX DAYS

Dog 14.—A black and white spotted hound weighing 17.4 Kg. was used. After the usual preparation, osteotomy of the right radius was done, with application of a plate and screws, on Dec. 3, 1936. With the dog under ether anesthesia induced by the open method the right radius was exposed through a muscle-separating anterolateral approach. Towels were held on the skin with clips. The periosteum was stripped, and a fracture was made with a large osteotome. A no. 41 drill was used for the screw holes. A no. 11 plate (four holes) and four screws (nos. 2, 4, 5 and 3) were used. The no. 2 screw and the no. 3 screw engaged one cortex only; the no. 4 screw and the no. 5 screw engaged both cortices. Rigid fixation in good position was obtained. The wound was closed in three layers.

On December 5 the animal was lively. There was not much edema. The dog did not use the paw.

On December 9 there was no weight bearing.

On December 16 the leg bore weight and the wound was healed.

On December 21 the dog was in excellent condition.

On December 4, 1937, the animal was killed. The skin was healed; the muscle planes were healed. The plate and screws were covered with a thin, fibrous membrane, through which the plate shone.

The following data were recorded:

No. 2 screw..... Short; very difficult to remove; may have lost substance in process of removal
0.2971 Gm. at operation
0.2960 Gm. at removal

0.0011 Gm. loss
0.3 per cent loss

No. 3 screw.....	Short; difficult to remove
	0.3021 Gm. at operation
	0.3014 Gm at removal
	0.0007 Gm. loss
	0.2 per cent loss
No. 4 screw.....	Long; impinged on ulna; easy to remove; friable tissue beneath plate at screw site
	0.4675 Gm. at operation
	0.4670 Gm. at removal
	0.0005 Gm. loss
	0.1 per cent loss
No. 5 screw.....	Long; moderately difficult to remove
	0.4773 Gm. at operation
	0.4765 Gm. at removal
	0.0008 Gm. loss
	0.1 per cent loss

PROTOCOL ON AN ANIMAL KILLED AT TWO YEARS AND ONE MONTH

Dog 12.—A brown and white spotted hound bitch weighing 16.6 Kg. was used.

On Dec. 9, 1936, osteotomy of the right radius was done, with application of a plate and screws. The lateral approach was developed to the proximal and middle third of the right radius. Towels were used on the skin. The periosteum was stripped with a blunt elevator, and the fracture made with a bone-cutting forceps and an osteotome. The fracture was reduced and held. A no. 41 drill was used for holes. A screw plate and four screws were used for fixation, which was fairly rigid. The incision was closed in the muscular and aponeurotic planes with interrupted silk sutures. The skin was closed as well.

On December 16 the leg bore weight. The wound was healing. There was very little edema.

On Jan. 21, 1937, the wound was healed. The leg bore weight. There was no edema.

On June 25 there was periodic development of a sinus at the upper limit of the scar, with rehealing. The plate was palpable. The animal was active. The leg bore full weight.

On June 2, 1938 it was noted the sinus occasionally still reopened. The animal bore a litter of pups. The plate was palpable. The upper end of the plate was loose. Rotation of the leg was painless.

On Jan. 9, 1939 the animal was killed. Pronation and supination of the injured leg were equal to those observed on the other side. There was no frank exudate. The sinus did not go to the plate. The plate was loose at the upper end. The proximal three screws were removed with ease. The distal screw was fairly firm. The plate and screws were completely covered with a fibrous envelope.

The following data were noted:

No. 11 plate	1.1891	Gm. at operation
	1.1870	Gm. at removal
	0.0021	Gm. loss
	0.1	per cent loss
No. 1 screw	0.2895	Gm. at operation
	0.2890	Gm. at removal
	0.0005	Gm. loss
	0.1	per cent loss
No. 6 screw	0.4876	Gm. at operation
	0.4869	Gm. at removal
	0.0007	Gm. loss
	0.1	per cent loss
No. 7 screw	0.4554	Gm. at operation
	0.4547	Gm. at removal
	0.0007	Gm. loss
	0.1	per cent loss
No. 9 screw	0.2898	Gm. at operation
	0.2890	Gm. at removal
	0.0008	Gm. loss
	0.2	per cent loss

OBSERVATIONS ON THE CLINICAL USE OF HIGH CHROMIUM, LOW NICKEL STEEL

The lack of evidence of electrolytic corrosion or loss of weight of the screws and plates in animals encouraged its use clinically. Well over 100 patients have been treated since the fall of 1936 with operative fixation. This was done by various members of the staff of the fracture service. Forty-two cases observed in 1937 and 53 observed in 1938 are considered here, not to evaluate them clinically or for end results but to extend observations on the use of the particular metal in question.

In 1937, 41 fractures were treated with fixation by the high chromium, low nickel steel plates and screws. Of these, 10 were humeral, 11 tibial, 8 femoral, 6 ulnar, 3 combined tibial and fibular with separation of the mortise, 2 radial and 1 acetabular.

Of the 41 cases, plates and screws were removed in 12. There were 6 compound injuries from which the plates and screws were removed. Four were fractures of the elbow with superficial plates, 1 a tibial fracture with a superficial plate and a persisting sinus and 1 a supracondylar fracture of the femur in which fixation was insecure and the plate and

screws were easily accessible. Of the 6 clean fractures from which the steel was removed, fixation was insecure in 4. One case may be excluded on the basis that a wire of dissimilar composition had to be used to secure the coronoid process in a complicated fracture of the elbow. From only 1 of the fractures operated on, not compounded and adequately fixed, was the fixative apparatus removed. This was a fracture of the midshaft of the femur, fractured six months before and treated nonoperatively elsewhere. The femur was fixed on Aug. 14, 1937. Five months after operation and one month after discarding the walking brace the patient noticed a mild ache at the site of operation. Seven months after operation a suture was expelled at the lower limit of the scar. A sinus persisted, and the plate was removed on June 20, 1938. Culture of material from the sinus showed Staphylococcus albus. At operation the tissue at the lowermost screw showed a brownish black granular discoloration. The culture was sterile, and the operative site did not connect with the sinus tract.

In the 53 cases with 57 bones treated operatively in 1938 and considered here, there occurred 11 fractures of the humerus, 12 of the tibia, 6 of the ulna, 10 of the radius, 5 of both the tibia and the fibula with separation of the mortise, 5 of the metacarpal bones, 1 of the phalangeal bones and 7 of the femur. Six were compounded wounds. From 2 of the last-mentioned fractures the plates and screws were removed after bony union because of persisting sinuses. One was a tibial fracture in which the plate had been superficially placed for expediency. The other was a femoral fracture operated on ten days after injury and treated elsewhere with débridement and closure of the wound. Both progressed to bony union, although a sequestrectomy was required before the femoral fracture wound healed. The 4 compound fractures from which the steel was not removed but which healed were 2 ulnar injuries, 1 tibial fracture and 1 metacarpal fracture.

Of the 6 clean fractures from which the plates and screws were removed, 3 showed insecure fixation with partial pulling out of screws (2 femoral fractures and 1 ulnar fracture). From 1 metacarpal fracture the plate and screws were removed incidentally to the removal of a painful spike of bone which persisted after the fracture had healed. Two clean tibial fractures from which the plates were removed, though the fixation was secure, showed clinical evidence of irritation. Both had been treated with materials which were not properly prepared. That is, the plate and screws had not been buffed and passivated, because production had changed from a handicraft basis to machine production. From 1 of these the plate and screws were removed five months after operation; from the other, ten months after operation. There was definite evidence of tissue irritation. Foci of corrosion were found along the

thread grooves of the screws or in the shank of the screw, where the finishing turn of the threading tool had left a small recess in which foreign materials collected. The only plate that showed corrosion was one in which the corroding screw shank was in contact with the screw hole. Some corrosion also occurred in screws which were driven off center, the threads being partially stripped against the plate hole.

In recapitulation of the clinical use of high chromium, low nickel steel, the following data may be noted. Of the 98 bones operated on and fixed internally, removal of the fixative device was attributable to the steel itself in 3. In all 3 the material had been improperly prepared. With the 21 other bones from which the steel was removed either for lack of rigid fixation or in the presence of a compound wound or infection, corrosion was a negligible factor in removal.

It is interesting that in 1937, except for 2 tibial fractures in patients who died of other injuries, the fixation material was removed eventually from all compound injuries, i. e., in 6. Of the 6 compound fractures observed in 1938, the wounds healed over the plates and screws in 4.

SUMMARY

A high chromium, low nickel stainless steel alloy has been used experimentally in dogs and clinically for internal fixation of fractures.

Certain adverse factors found in its use are discussed.

Some technically primary requisites are stressed.

CONCLUSION

When certain requirements are fulfilled, a high chromium, low nickel alloy is an adequate material physically, metallurgically and clinically for internal fixation of fractures.

SITUS INVERSUS TOTALIS AND DISEASE OF THE BILIARY TRACT

SURVEY OF THE LITERATURE AND REPORT OF A CASE

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Transposition of viscera has been recognized since the days of Aristotle (who recorded observations on 2 instances of transposed organs in animals), but it was not until 1600 A. D. that Fabricius described a a case of reversed liver and spleen in the human being.[1] Petrius Servius recorded a case of transposition of the viscera in 1615,[2] and Kuchenmeister (1824) first recognized the condition in a living person.[1] Subsequent to this clinical pioneering, sporadic cases were reported throughout the literature, but the true incidence was not appreciated until the modern era began, in 1897, with Vehsemeyer's [3] demonstration of transposition by means of the roentgen rays. This mode of examination has made confirmation of the anomaly relatively simple, and the incidence of reported cases has increased accordingly. Cleveland,[4] in 1926, found approximately 400 cases of transposition in the literature, and Larson [5] estimated that there have been 75 cases reported since that time.

There is considerable variation in the frequency of this anomaly as reported by different authors. Thus, Sherk [2] reported 10 instances in 347,000 registrations at the Mayo Clinic in the preceding twelve year period. Lewald [6] observed the condition 29 times in roentgen examinations of the chests and gastrointestinal tracts of 40,000 patients. Cleve-

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1. Lineback, P. E.: An Extraordinary Case of Situs Inversus Viscerum Totalis, J. A. M. A. **75**:1775 (Dec. 25) 1920.

2. Sherk, H. H.: Total Transposition of Viscera, Surg., Gynec. & Obst. **35**:53, 1922.

3. Vehsemeyer: Ein Fall von congenitaler Detiokardie; zugleich ein Beitrag zur Verwerthung der Röntgenstrahlen in Gebiete der inneren Medizin, Deutsche med. Wchnschr. **23**:180, 1897.

4. Cleveland, M.: Situs Inversus Viscerum: Anatomic Study, Arch. Surg. **13**:342 (Sept.) 1926.

5. Larson, C. P.: Situs Inversus with Other Congenital Anomalies, Canad. M. A. J. **39**:474, 1938.

6. Lewald, L. T.: Complete Transposition of Viscera, J. A. M. A. **84**:261 (Jan. 24) 1925.

land [4] reported observing 1 example in 10,000 routine dissections, and Rösler [7] recorded 3 observed in 22,402 autopsies. Adams and Churchill [8] stated that situs inversus was diagnosed in the cases of 23 of a total of 232,112 patients admitted to the Massachusetts General Hospital, an incidence of 0.002 per cent of the hospital population. Balfour [9] wrote that 51 cases of situs inversus have been encountered at the Mayo Clinic over a period of twenty-one years. Cockayne [10] stated the ratio of males to females with complete transposition to be 32:27 and added that the condition has been reported as occurring in all races except the Australoid.

NATURE OF TRANSPOSITION OF THE VISCERA

Transposition of viscera may be either partial or complete. The complete form has often been thought of as a mirror image of the normal, left handedness, position of the testes, etc., being used as criteria. Cockayne's [10] study, however, shows no greater incidence of left handedness in patients with situs inversus than in normal persons, and so it cannot be assumed that the central nervous system, or at least that portion concerned with the determination of manual dexterity, shares in the transposition. Actually, the condition is best thought of as an abnormal (sinistral) rotation of the thoracoabdominal viscera resulting in a reversal of the normal relations. For example, in complete transposition the anatomic arrangements are briefly as follows: [4] The heart lies to the right of the midline, and its chambers are reversed, the apex being the right ventricle, from which arises the aorta. The aorta arches toward the right, giving off the innominate artery (which subsequently divides into the left common carotid artery and the subclavian artery), the right common carotid artery and the right subclavian artery. The great veins empty into the left atrium, whence the blood passes into the left ventricle, the pulmonary arteries, the pulmonary capillary bed, the pulmonary veins and the right atrium, respectively. The thoracic duct lies to the right and empties into the right subclavian vein near its junction with the internal jugular vein. The lungs are structurally reversed, the right being bilobed and the left trilobed. Intra-abdominally, the cardia lies to the right of the midline and the lesser curvature extends toward the left. The spleen is on the right, and the gallbladder and liver (with reversal of the normal lobular arrangement of the

7. Rösler, H.: Beiträge zur Lehre von den angeborenen Herzfehlern, über die angeborene isolierte Rechtslager des Herzens, Wien. Arch. f. inn. Med. **19**:505, 1930.

8. Adams, R., and Churchill, E. D.: Situs Inversus, Sinusitis, Bronchiectasis, J. Thoracic Surg. **7**:206, 1937.

9. Balfour, D. C.: Personal communication to the authors, 1939.

10. Cockayne, E. H.: Genetics of Transposition of the Viscera, Quart. J. Med. **7**:479, 1937.

latter), on the left. The entire intestinal tract is reversed, with the cecum and appendix on the left and the sigmoid flexure of the colon in the right iliac fossa.

Partial transposition is known to occur in three main forms, although gradations between the types are so common as to make definite classification difficult. Thus, one may have partial transposition of both the thoracic and the abdominal organs, transposition affecting the abdominal organs alone or dextrocardia alone. In the last-mentioned condition the normal chambers of the heart are reversed as is the location of the organ.

The relation between the various forms of partial transposition and total transposition is imperfectly understood, although in many of the reported cases there were gradations toward the complete which would make one suspect that the differences are more apparent than real. That is, all of the changes may be the result of the same fundamental process, the chief difference being one of degree.

ORIGIN

The nature of situs inversus has aroused the curiosity of medical investigators since the time of its original description, and speculations as to its origin have run the gamut of medical imagination, from the supernatural views of Aristotle, who considered it a visitation from the gods,[11] to the more elaborate embryologic explanations of recent years. Many of the latter have little or no evidence to support them, and chief among these are the hypotheses based on the assumption that the location of the viscera is determined by the course of their blood supply or by variations in their hemodynamics during the formative period. We shall attempt to focus our attention on the more fundamental of the factual theories.

In general, variations from normal development may be thought of as arising either from causal elements inherited in the germ plasm or from changes in the environment of the fertilized ovum. Studies of the former (the genetics of transposition) have for the most part been confined to analyses of the families of persons with situs inversus, whereas study of the "acquired" form has consisted of attempts to produce developmental abnormalities through changes in the external influences which act on the embryo during its earliest stages. Confirmatory evidence has been collected by the advocates of both views, and this evidence will be briefly presented. It should be remembered that the exponents of the heredity theory have the tremendous advantage of being able to arrive at their conclusions as the result of study of

11. Beck, C.: Case of Transposed Viscera with Cholelithiasis Relieved by a Left-Sided Cholecystostomy, Ann. Surg. **29**:593, 1899.

the condition in human beings, whereas the supporters of the theory that the condition is acquired must rely on evidence collected from their observation of lower forms. Deductions drawn from animal experimentation are, as is well known, not always applicable to the human being.

For many years the attention of workers has been drawn to the not infrequent occurrence of transposition in monsters. Since in double monsters one often exhibits complete or partial transposition, it has been suggested that situs inversus represents monozygotic twinning with absorption of the normal fetus. If this were the true mechanism, one would expect to find many identical twins with reversal of viscera. Wilder [12] studied this problem, and he found that, although double monsters often exhibit many different degrees of visceral transposition, duplicate twins have only a few minor integumentary reversals, such as "mirror imaging" of the fingerprints of particular fingers. He considered these mirror reversals of normal symmetry as vestigial remains of a more generalized transposition in early fetal life. Newman [13] found reversal of tegumentary patterns in armadillo quadruplets and expressed the belief that the relatively greater tendency toward reversal seen in these animals (and in monsters) was due to their separation late in ontogeny; human identical twins separate early.

Spemann [14] and Pressler,[15] working separately with Bombinator igneus in the neurula stage, found that by surgically reversing a section of the medullary plate together with a portion of the roof of the primitive gut situs inversus could be produced in many instances.

Stockard [16] was able to produce certain deformities by varying the environment of Fundulus eggs. His work was based on the assumption that a given species develops at a specific rate, which is probably dependent on the rate of protoplasmic oxidation in that particular species. Experimentally, this oxidative rate could be varied either by lowering the temperature or by decreasing the supply of available oxygen; by thus altering the rate during certain periods when there was marked inequality of growth in different parts of the embryo,

12. Wilder, H. H.: Duplicate Twins and Double Monsters, Am. J. Anat. **3**: 387, 1904.

13. Newman, H. H.: Heredity and Organic Symmetry in Armadillo Quadruplets, Biol. Bull. **30**:173, 1916; Experimental Studies of Asymmetry in the Starfish, Patiria Miniata, ibid. **49**:111, 1925; Studies of Human Twins, ibid. **55**: 283, 1928.

14. Spemann, H.: Ueber embryonale Transplantation, Verhandl. d. Gesellsch. deutsch. Naturf. u. Aertzer, 1906, p. 189.

15. Pressler, K.: Beobachtungen und Versuche über den normalen und inversen Situs Viscerum et Cordis bei Anurenlarven, Arch. f. Entwcklngsmechn. d. Organ. **32**:1, 1911.

16. Stockard, C. R.: Structure and Developmental Rate, Am. J. Anat. **28**:115, 1921.

almost any type of deformity could be produced. The type of monster produced was dependent on the stage of embryonic development at which the inhibiting environment was applied, and, in general, the greatest deformity developed in those organs in which growth was most rapid at the time of inhibition.

Newman [18] studied the effects of low temperatures on the development of Patiria miniata. He found that "icing" before or during early cleavage resulted in a high incidence of twins, "icing" at the blastula stage produced an increase in the percentage of larvae showing reversed, or right-handed, symmetry and similar cooling at other developmental stages resulted in different but equally striking results. In his opinion, reversal of symmetry is simply the specific effect resulting from arrest of growth of the larvae at the blastula stage.

The heredity theory has been somewhat strengthened by observations on insects that rotation may be caused by a gene. Thus, Sumner and Huestis,[17] working with a mutant of Drosophila melanogaster in which the tip of the abdomen was rotated counterclockwise, found that this was determined by a recessive gene in the third chromosome. Other investigators have found somewhat similar but different genes of rotation in this same species.

Cockayne's [10] comprehensive study of a fairly large number of human families showed that "complete transposition of the viscera agrees with what is expected of a rare recessive character in its familial incidence and general distribution within a family, in its occurrence in both members of a pair of monozygotic twins whose parents are normal, in the high percentage of first cousin marriages that give rise to it and, insofar as can be determined, in the ratio of affected to normal children in fraternities." His analysis revealed that other developmental abnormalities, such as congenital heart disease, are more common in persons with transposition than among the general population and that this liability to defective development is much greater with partial than with total transposition. He concluded that complete transposition is inherited as a recessive character determined by a single autosomal gene, and in his opinion partial transposition is probably determined by the same gene. The higher incidence of associated anomalies results in the classification of this gene with the partially lethal group.

Adams and Churchill,[8] in attempting to correlate these divergent findings, offered the suggestion that there may be two types of person with transposition of the viscera: the true mutant, in whom the tendency toward transposition is inherited as a recessive character, and the true monster, in whom the transposition is the result of external influences acting after fertilization. The former would be expected to

17. Sumner, F. B., and Huestis, R. R.: Bilateral Asymmetry and Its Relation to Certain Problems of Genetics, Genetics **6**:445, 1921.

be perfectly normal except for the transposed viscera; the latter would probably have other developmental abnormalities. This view, while admittedly hypothetic, does aid in evaluating these apparently different clinical types.

DIAGNOSIS OF TRANSPOSITION OF THE VISCERA

Recognition of total transposition or those forms of partial transposition in which the heart is on the right is comparatively simple. The apical impulse and the heart sounds are usually readily discernible on the right, and the cardiac outline on percussion is discovered to the right of the midline. Not infrequently the liver or the spleen may be found reversed on palpation and percussion. Roentgen examination will confirm these findings and, with the aid of complete gastrointestinal studies and cholecystograms, will reveal the transposed abdominal contents. Dextrocardia results in an electrocardiogram in which there is total inversion of lead I and transposition of leads II and III.[18]

Surgical interest in situs inversus is confined almost entirely to the abdomen, and it is here that its early recognition becomes of the utmost importance. As has been mentioned, the available evidence is against the view that the central nervous system shares in the transposition, and it is both interesting and confusing that in many of the reported cases of acute appendicitis associated with transposition there were symptoms referable to the right lower quadrant of the abdomen. In 1935, Pol collected a total of 46 cases of appendicitis on the left side, associated with partial or complete transposition, and in more than one half of these cases the pain was localized on the right side.[19] In only 7 of the 46 cases was the correct diagnosis made preoperatively. Block and Michael[19] agreed with Kuntz, whom they cited, in explaining this on the assumption that although the viscera are transposed their nerve supply is the same, so that referred pain from the diseased viscus is localized in the somatic area supplied by nerves connected with the same segment of the nervous system as those to the viscus. This discrepancy in symptoms does not seem to be so pronounced with diseases affecting the biliary tract, and, although atypical symptoms are not uncommon, the pain usually is localized in the left upper quadrant and radiates toward the left scapula.

In cases of obvious total transposition the false localizing symptoms resulting from referred pain may be correctly interpreted and serious diagnostic error avoided, but in cases of only partial abdominal transposition laparotomy is often necessary in order to establish a diagnosis.

18. Waller, A. D.: On the Electromotive Changes Connected with the Beat of the Mammalian Heart and of the Human Heart in Particular, Phil. Tr. Roy. Soc., London **180**:169, 1889.

19. Block, F. B., and Michael, M. A.: Acute Appendicitis in Complete Transposition of Viscera, Ann. Surg. **107**:511, 1938.

This is true particularly when the clinical picture is that of a surgical emergency and the condition of the patient such as to discourage delay.

The following case is one of situs inversus associated with cholecystitis.

REPORT OF CASE

A white woman aged 46, right handed, entered the Vanderbilt Hospital for the sixth time on July 10, 1939. The first admission was in February 1932, and the findings included pregnancy (the seventh), pyelitis, situs inversus and a mixed

Fig. 1.—Cholecystogram showing concentration of dye and gallstones. The gallbladder was in the left upper quadrant of the abdomen.

tumor of the parotid region. Electrocardiographic studies showed inverted T and P waves in leads I and II. The patient returned to the hospital in May 1935, at which time the mixed tumor of the parotid region was removed. Other findings included nontoxic nodular goiter, cystocele and rectocele. She was admitted to the hospital for the third time in February 1936, complaining of hematuria. Ureteral catheterization showed that the blood was coming from the left ureter, and a plain film revealed several indefinite shadows in the region of the left kidney. Pyelograms showed slight blunting of the minor calices. The patient improved after nonoperative therapy and was discharged. She was readmitted to the hospital several months later, at which time operations for correction of

the cystocele and rectocele were performed. The record of this admission contains the first description of pain, which she said she had first experienced sixteen years previously, shortly before the delivery of her fifth child. This and many subsequent attacks had consisted of pain in the epigastrium which radiated to the right flank. Each attack lasted several hours; the pain was severe, but morphine was not required. Hematuria had never been observed during the attacks. She stated that in recent years the frequency of the attacks had increased. In addition, she complained of pain in the lower part of the abdomen, which was separate and distinct from that in the upper part. She returned to the outpatient clinic several months subsequently, stating that she had had difficulty in breathing and that she wished to have the goiter removed. A nontoxic adenoma of the thyroid was removed on June 29. After discharge, she returned to the outpatient clinic on a number of occasions because of pain and swelling of her legs and obesity. On June 15, 1939, she stated that she had had severe abdominal pain four days previously which was similar to that which she had had intermittently

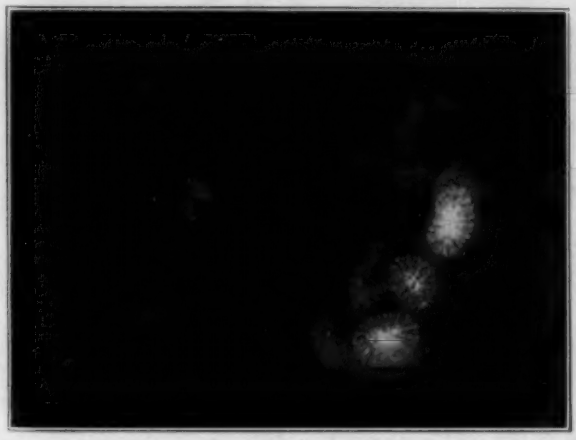

Fig. 2.—Postoperative roentgenograms of the gallbladder and appendix.

for sixteen years. The attacks were described as beginning with discomfort in the epigastrium followed by sudden sharp stabbing pains, usually in the right side of the epigastrium, with radiation to the right flank and to the back. The attacks were accompanied by severe nausea with eructation of gas and yellowish liquid but no frank vomiting. Jaundice had never been observed. Buttermilk and fried potatoes were the only foods which she had noticed as apt to bring on an attack. Intravenous cholecystographic examination showed good concentration of the dye and several opaque stones in the gallbladder, which was situated in the left upper quadrant of the abdomen (fig. 1). Examination of the intestinal tract after a barium sulfate meal and a barium sulfate enema revealed no abnormality other than transposition.

With the patient under nitrogen monoxide, oxygen and ether anesthesia (endotracheal), operation was performed on July 13. A small paramedian incision was made, and the muscle was retracted laterally. Complete transposition of all the abdominal viscera was verified. The liver was almost entirely on the left, there being a thin layer of liver tissue on the right. The spleen was located just beneath the right side of the diaphragm. The appendix was in the left lower quadrant

of the abdomen. It was removed, and the stump was inverted. There were many adhesions about the gallbladder, which was slightly grayish and contained stones. There was scarring of the liver in the neighborhood of the attachment of the gallbladder. After the adhesions about the gallbladder had been freed, the organ was removed from below upward, the cystic duct and vessels being ligated separately. The common duct was not dilated. A cigaret drain was inserted, and the incision was closed. The gallbladder contained three rather large calcium, bilirubin and cholesterol stones. A roentgenogram (fig. 2) was taken of the gallbladder after removal.

The patient was discharged from the hospital sixteen days after the operation. She has returned to the outpatient clinic on several occasions for observation, and there have been no further complaints of pain or indigestion.

COMMENT

Reported cases of lesions of the biliary tract in association with situs inversus are few. A fairly comprehensive survey of the literature reveals only 17 reported as such, and in several of these the diagnosis has not been proved either roentgenographically or at operation. These cases are presented in brief in the accompanying table. It will be noted that in several cases a slight icteric tint was reported, but unless a definite diagnosis of jaundice was made this condition was incorporated in the table as questionable. The results of cholecystographic study are available, naturally, only in cases observed since 1924, when the method was first introduced by Graham and Cole.

Only 1 of the 9 patients in whose cases the information was given was left handed. Ten were females, and 7 were males; the sex of 1 was not mentioned. In 11 of the 16 cases in which the location of pain and tenderness was mentioned, the left upper quadrant of the abdomen and the back were the major points of involvement. In 2 instances most of the discomfort was on the right side, and in 3 it was in the epigastrium. These figures show that the tendency of pain to be referred to the right from a viscus transposed to the left is not so great with cholecystitis as with appendicitis. As has been stated, in more than one half of the cases of appendicitis associated with situs inversus there are localizing signs indicative of disease in the right lower quadrant of the abdomen. Our patient is one of only 2 with disease of the gallbladder and situs inversus in whom most of the discomfort was in the right upper quadrant. These facts make the anatomic and pathologic diagnosis of "left-sided" cholecystitis somewhat easier than that of "left-sided" appendicitis. Furthermore, one is usually warranted in allowing a longer period for observation and study of patients in whose cases cholecystitis is suspected than of those for whom acute appendicitis is feared.

There is no evidence to indicate that disease of the biliary tract is more common in persons with situs inversus than in the general popu-

Author	Patient	Duration and Nature of Symptoms
Beck [11]	White woman aged 39; sextipara; left handed	14 years of headaches and colicky pain in left lumbar region
Billings, F.: Two Interesting Cases, Philadelphia M. J. **6**: 670, 1900.....	White man aged 64; right handed	5 years of intermittent pain, indigestion, chills, fever and jaundice
*Mayo, W. J., in Keen, W. W.: Surgery: Its Principles and Practice, Philadelphia, W. B. Saunders Company, 1914, vol. 3, p. 969	.....	Mentioned case but gave no history
Kehr, H.; Liebold, and Neuling: Drei Jahren Ballenstein Chirurgie. Bericht über 312 Laparotomien am Gallensystem aus den Jahren 1904-1906, Munich, J. F. Lehmann, 1908, p. 329	Man aged 55	13 years of intermittent colicky pain in left upper quadrant of abdomen
Hupp, F. L.: Malpositions of the Liver, New York M. J. **94**: 423, 1911.....	Woman; bipara; 3 times pregnant; right handed	4 years of intermittent pain, jaundice and loss of weight
Horn, H. W.: Situs Viscerum Inversus with Gallstones, Ann. Surg. **62**: 424, 1915.....	White woman aged 51; quadripara	30 years of dull, aching pain, indigestion and eructation
Kelly, R. E.: Transposition Associated with Gallstones and Hourglass Stomach, Brit. J. Surg. **8**: 137, 1920	Woman aged 40; bipara; right handed	3 years of colicky pains related to ingestion of food and relieved by vomiting
Bell, G., and Winn, R. C.: Cholecystitis in a Patient with Transposition of Viscera, M. J. Australia **1**: 339, 1920	Man aged 37; right handed; right testicle lower	24 hours of severe pain
Frischmann, E. S.: Cholelithiasis with Situs Inversus, Brit. M. J. **2**: 811, 1923.....	Woman aged 43; tripara; right handed	3 months of intermittent pain with jaundice
Bettman, R. B., and Binswanger, H. F.: Cholecystitis Associated with Situs Transversus, Am. J. M. Sc. **172**: 570, 1926	Man aged 49; right handed	Few hours of excruciating pain, with a history of 2 similar attacks in past
Galíndez, A., and Delrío, J. M.: Síndrome coledociano y periduodenitis en una transposición total de vísceras, Bol. y trab. de la Soc. de cir. de Buenos Aires **14**: 1011, 1930	Man aged 28; right handed; left testicle lower	Since childhood, epigastric pain relieved by food; few months of attacks of pain in left upper abdominal quadrant and jaundice
Counseller, V. S.: Rupture of Spleen, Gunshot Wounds of Abdomen, Transposition of Organs: Report of Cases, Proc. Staff Meet., Mayo Clinic, **6**: 504, 1931	Man aged 28	2 years of intermittent pain and frequent eructation; acute pain shortly before admission
Carnot, P.: Coliques hépatiques à gauche dans un case d'inversion viscérale, Paris méd. **2**: 537, 1931	Woman aged 32; bipara	3 months of intermittent colicky pain in left upper abdominal quadrant
Beltrametti, L.: Sopra un caso di colecistite probabilmente calcolosa in soggetto con situs viscerum inversus totalis, Gior. de clin. med. **14**: 93, 1933	Girl aged 17	6 months of intermittent pain occasionally associated with vomiting and fever
Troutt, J. M.: Situs Transversus Viscerum—Case with Cholelithiasis, Ann. Surg. **98**: 1109, 1933	Woman aged 45	Not stated
Tirczka, C.: Cholecystektomie bei Situs inversus totalis, Zentralbl. f. Chir. **61**: 1172, 1934	Woman aged 40	6 years of intermittent cramping pain with indigestion and loss of weight
Barú, R. J., and Isasi, E.: Inversion total de vísceras; litiosis biliar y pequeño quiste hidático intrahepático, Arch. urug. de med., cir. y especialid. **9**: 191, 1936	Man aged 24	Obstinate constipation for 16 yrs.; intermittent pain, nausea, vomiting, indigestion and eructation for 8 months

* In a recent communication Balfour [9] stated that the operation mentioned was performed for an intermittent intestinal obstruction secondary to a retroperitoneal dermoid and that the findings in the gallbladder were incidental.

Pain		Findings	Complications	Preoperative Diagnosis of Transposition	Roentgen Confirmation		Operation	Results
Location	Radiation				Transposition	Disease of Gallbladder		
Left lumbar region	No	Palpable left kidney and resistance at left costal margin	Ptosis of left kidney	Yes	Yes	No calculi noted	Nephropexy (left) and subsequently cholecystostomy with removal of 4 stones	Uneventful recovery
Epigastrium	No	Hard mass at left costal margin	Obstructive jaundice	Yes	No	No	Cholecystostomy with removal of one large stone from cystic duct	Death 4 days after operation
Left upper abdominal quadrant	No	No tenderness	Chronic productive cough; obstructive jaundice	Yes	Yes	No calculi noted	Stone removed from common duct; drainage of common duct	Uneventful recovery
Epigastrium	To left	Tenderness over entire epigastrium	4½ months' pregnancy; obstructive jaundice	No	No	No	Cholecystostomy with removal of 2 stones from the cystic duct	Uneventful recovery and subsequent normal delivery
Left upper abdominal quadrant	To left scapula	Tenderness in left upper quadrant of abdomen	.....	Yes	Yes	No calculi noted	Cholecystostomy with removal of 4 stones	Uneventful recovery
Epigastrium and right upper abdominal quadrant	To right scapula	.....	Hourglass stomach from ulcers on lesser curvature	Yes	Yes	No calculi noted	Posterior gastroenterostomy and cholecystectomy; gallbladder full of stones	Uneventful recovery
Left upper quadrant of abdomen	No	Marked tenderness and rigidity of left upper quadrant of abdomen	Syphilis of 12 years' duration	Yes	Yes	No calculi noted	Cholecystostomy; gallbladder was acutely inflamed and contained one large stone	Secondary cholecystostomy performed on 37th postoperative day with recovery
Left upper quadrant of abdomen	To back and left shoulder	Indefinite tender mass in left upper quadrant of abdomen	Obstructive jaundice	Yes	Yes	No calculi noted	Cholecystectomy and choledochotomy with removal of stones from both gallbladder and common duct	Subsequent course uneventful
Left upper quadrant of abdomen	To left scapula	Tenderness and rigidity in left upper quadrant of abdomen	Jaundice ?	Yes	Yes	Shadow of gallbladder seen on left; no calculi noted	Refused	Improvement after 3 days' hospitalization
Epigastrium and left upper quadrant of abdomen	No	Tenderness in left upper abdominal quadrant with tender palpable liver on left	Jaundice ?	Yes	Yes	No calculi noted: cholecystogram not mentioned	Cholecystectomy and appendectomy; gallbladder contained no stones	Uneventful recovery
Epigastrium	Not mentioned	Rigidity in left upper quadrant of abdomen	.....	Yes	Yes	Cholecystogram: gallbladder nonfunctioning	Cholecystectomy and appendectomy; gallbladder contained many stones	Uneventful recovery
Left upper quadrant of abdomen	To left scapula and shoulder	Tenderness at left costal margin	Jaundice ? ("subicterus")	Yes	Yes	Cholecystogram showed gallbladder on left; no stones	None; medical regimen instituted	Not stated
Epigastrium and left upper quadrant of abdomen	To left scapula on 1 occasion	Tenderness in left flank with palpable liver on the left	.....	Yes	Yes	Cholecystogram; gallbladder did not visualize; no stones	Refused	Not stated
Not stated	Not stated	Not stated	(1) Chronic arthritis; (2) chronic pyelitis	Yes	Yes	Multiple faceted stones	Cholecystectomy and appendectomy	Uneventful recovery
Left upper quadrant of abdomen	Not stated	Fist-sized mass in left upper quadrant of abdomen	.....	Yes	Yes	Calculi not noted	Cholecystectomy; gallbladder contained stones	Uneventful recovery
Left upper quadrant of abdomen	To left side of back	Generalized tenderness and spasticity	Intrahepatic hydatid cyst; jaundice ?	Yes	Yes	Cholecystogram: gallbladder did not fill; intrahepatic cyst seen	Not stated	Not stated

lation. Although situs inversus is usually perfectly compatible with normal health and longevity, there is some evidence that persons with this condition have a higher percentage of congenital abnormalities. The findings of Kartagener [20] and those of Adams and Churchill [8] show conclusively that the incidence of bronchiestasis in persons with situs inversus is markedly increased. The latter authors stated: "The incidence of bronchiectasis in the 23 cases (Massachusetts General Hospital) of situs inversus is 21.7 per cent. The incidence of bronchiectasis in the hospital population is 0.036 per cent. The incidence of situs inversus in the hospital population is 0.002 per cent." One of the 5 patients with situs inversus observed in the Vanderbilt Hospital in the past twelve years had bronchiectasis.

SUMMARY

Seventeen cases of situs inversus and disease of the gallbladder have been found in the literature, and an additional case is reported. The pain of appendicitis in a person with transposition of the viscera is usually on the right side; the pain of disease of the gallbladder is usually on the left. As a result of studies on appendicitis, cholecystitis, bronchiectasis and other diseases, the status of situs inversus has changed from that of an anatomic curiosity to that of a clinically important entity. Its early recognition is very important in some surgical emergencies.

20. Kartagener, M.: Zur Pathogenese du Bronchiektasien, Beitr. z. Klin. d. Tuberk. **83**:489, 1933; **84**:73, 1933; **87**:331, 1935.

SURGICAL TREATMENT OF SIGMOIDOVESICAL FISTULAS

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The creation of a sigmoidovesical fistula by a process primary in either the sigmoid flexure of the colon or the urinary bladder is a serious complication which fortunately confronts the surgeon only infrequently. It engenders so poor a prognosis that the choice of treatment must be guided by great care, for the mortality resulting from surgical attack is extremely high. The pathologic entity responsible for the formation of such an abnormal channel is usually primary in the sigmoid and but rarely has its origin in the bladder. Occasionally an inflammatory process external to both sites may be the responsible agent. Parham and Hume,[1] Sutton[2] and Kellogg[3] have each presented excellent classifications of the causes of sigmoidovesical fistula.

The frequency of communication between the sigmoid flexure of the colon and the urinary bladder as compared to other intestinovesical fistulas has gradually increased since the earlier reports. Pascal[4] found involvement of the sigmoid flexure in 18 per cent, Albano[5] in 45 per cent, Sutton in 57 per cent and Kellogg in 63 per cent of their respective series. In a review of 385 cases, Parham and Hume reported that in only 33 cases (11 per cent) were sigmoidovesical fistulas observed in the 278 patients with enterovesical fistula for whom the location of the lesion was stated. Higgins[6] has reported that the sigmoid flexure and the urinary bladder were involved 95 times in a total of 406 cases of vesicointestinal fistula.

From the Division of Surgery, the Mayo Clinic.

1. Parham, F. W., and Hume, J.: Vesico-Intestinal Fistulae, Ann. Surg. **50**: 251-286 (July) 1909.

2. Sutton, C. D.: Vesicosigmoidal Fistulae, Surg., Gynec. & Obst. **32**:318-327 (April) 1921.

3. Kellogg, W. A.: Vesico-Intestinal Fistula, Am. J. Surg. **41**:135-186 (July) 1938.

4. Pascal, cited by Kellogg.[3]

5. Albano, G.: Contributo clinico allo studio delle fistole vescico-intestinali, Arch. ital. di chir. **16**:133-172, 1926.

6. Higgins, C. C.: Vesico-Intestinal Fistula, J. Urol. **36**:694-709 (Dec.) 1936.

Although slight variations due to the causative factor may be present, the general syndrome presented by patients with sigmoidovesical fistula is essentially constant. As a rule, those with diverticulitis state that the condition was gradual in onset. Repeated attacks of pain in the left lower abdominal quadrant, abdominal cramps and left iliac tenderness occur because of the diverticulitis. Simultaneously with the last-mentioned symptom, or perhaps later in the course of events, burning and frequency of urination occur. Micturition may occur hourly and may be accompanied by a scalding pain either during or at the completion of the act. Chills and elevations of temperature complete the syndrome of sigmoidovesical fistula.

With the establishment of fistula into the bladder, bubbles of gas may be passed through the urethra, usually at the end of micturition, but the passage of feces does not occur as frequently as does that of flatus. The fecal content of the urine is conditioned by the state of the bowels, for when they are in a constipated state little or no feces will be seen. However, the onset of fluid stools increases the quantity of fecal material in the urine. In some patients the start of all their difficulty is marked by a gush of air and feces through the urethra. When the ordinary flow in such a fistula is reversed and the urine is diverted into the bowel, slight laxity of the bowels or chronic diarrhea may result.

Symptoms referable to the urinary bladder alone were present in 8 patients with fistula. Only after careful examination was the true etiologic factor in the colon discovered. Six patients with diverticulitis of the sigmoid flexure and 2 with a malignant lesion in the same locality complained only of symptoms associated with cystitis. Conversely, an occasional patient, like 1 of those with a malignant lesion in the present series, may give no subjective information and have no objective signs when a fistula is present, except a little pus or blood in the urine. The communication is discovered only when exploratory laparotomy is performed.

From the diagnostic standpoint, a history of passage of gas and feces through the urethra is pathognomonic. Instances have been reported in which an unsuspected opening into the bladder was found on cystoscopic examination, but this occurs infrequently, and usually a definite history of difficulty with the bladder is obtained. The quantity of pus in the urine varies, and occasionally erythrocytes in small number are seen on microscopic examination of the urine. Gross hematuria is noted less frequently.

Cystoscopic examination, of course, is necessary and invaluable in the diagnosis. A fistulous opening, usually on the left side of the bladder, may be visualized, but frequently this is not seen, for a mass of granulation tissue or a depressed necrotic region in the bladder may be the

only evidence there that a fistula exists. By means of the cystoscope gas may be seen to bubble through the opening, and occasionally feces may exude. When a suspicion exists that a fistulous tract is present, a lead catheter may be passed gently through the necrotic region and a roentgenogram taken. The shadow cast by the catheter may then be seen in the colon. Force should not be used, as the possibility of creating a false passage is a definite menace. Cystograms may aid the diagnostician in that the mediums may outline the tract.

Methylene blue may be injected into either the bladder or the rectum and its passage from the corresponding location awaited. When a positive result is noted, conclusive proof of fistula is present.

Proctoscopic procedures, although a valuable aid in some cases, are not usually of much help in visualization of the intestinal opening of the tract. In most cases the aperture is too high to be seen; also, the inflammatory changes in the bowel may obscure the primary opening. However, by direct observation and perhaps a biopsy of material from the lesion, the proctoscopist many times can make a decision as to the etiologic agent.

Likewise, by indirect observation, the roentgenologist may state the correct nature of the lesion. He may also see the tract, outlined by barium sulfate, leading from the sigmoid flexure to the urinary bladder.

Pneumaturia, although helpful in the diagnosis of fistula, is not pathognomonic. The etiology of pneumaturia has been fully discussed by Kelly and MacCallum,[7] Hinman[8] and Riley and Bragdon.[9] Introduction of air into the bladder during catheterization or therapeutic procedures will result in its passage later, and this should be clearly distinguished from true pneumaturia. Gas entering the bladder from the intestinal tract is a second etiologic agent. Also to be demarcated from the group of patients with vesicointestinal fistula are those diabetic patients in whom the passage of gas through the urethra is the result of decomposition or fermentation of urine in the bladder by yeast organisms. In occasional cases of chronic infections of the renal pelvis or of the bladder pneumaturia may occur. The offending bacterial organisms include Escherichia coli, Aerobacter aerogenes and Coccobacillus vesicae.

Complicating the formation of a fistula are a number of secondary infections of the genitourinary system. Symptoms referable to cystitis are greatly increased at the time the fistula becomes complete. Pyelitis and pyelonephritis are of infrequent occurrence in spite of the number

7. Kelly, H. A., and MacCallum, W. G.: Pneumaturia, J. A. M. A. **31**:375-381 (Aug. 20) 1898.

8. Hinman, F.: The Principles and Practice of Urology, Philadelphia, W. B. Saunders Company, 1935.

9. Riley, F. G., and Bragdon, F. H.: Pneumaturia in Diabetes Mellitus: Report of a Case, J. A. M. A. **108**:1596-1599 (May 8) 1937.

of cases of necrotic cystitis observed. Likewise, the formation of stones in the bladder is rare. Of great importance is the psychologic effect on the patients of the passage of discharges through unnatural channels. This is true particularly of those patients who are reduced to a diaper era by rectal incontinence of urine. They become mentally depressed and despondent.

In 1921, Sutton reported from this clinic the cases of 34 patients with sigmoidovesical fistula. In this group there were 3 in whom the condition was due to trauma, 23 in whom it was due to inflammatory conditions exclusive of diverticulitis, 6 in whom it was due to diverticulitis and 2 in whom it was caused by carcinoma. If the present series is combined with that of Sutton, a total of 88 patients have been observed (table 1).

Certain comparisons between the two groups of patients are of interest. Sutton reported observing fistulas in 26 women and 8 men, while in the present series there were 9 women in contrast to 45 men.

TABLE 1.—*Etiologic Factors in Eighty-Eight Cases of Surgically Treated Sigmoidovesical Fistula*

Traumatic factors	3
Inflammatory factors	33
Diverticulitis	38
Carcinoma	14

This difference is accounted for by the fact that salpingitis, specific or nonspecific, was the etiologic factor in a majority of Sutton's series, while it was not encountered in the present series. However, fistulas due to diverticulitis have increased from 6 in Sutton's series to 32 in the present. A somewhat smaller increase has also been seen in the number of fistulas resulting from carcinoma.

Diverticulitis is perhaps the leading cause of sigmoidovesical fistula. Diverticula of the colon occur most frequently in the sigmoid flexure, and, according to Rankin and Brown,[10] a trifle more than 5 per cent of patients at the Mayo Clinic on whom roentgen studies of the colon were made were found to have diverticula. Rankin and Brown's statistics further reveal an incidence of diverticulitis in about 17 per cent of patients who had diverticula.

The pathologic sequence of events culminating in sigmoidovesical fistula due to diverticulitis may be reconstructed in the following manner. Once a diverticulum is formed, it tends to undergo progressive enlargement. With such progression, the muscular coat of the colon gradually disappears, and, since a small sac with a narrow neck is

10. Rankin, F. W., and Brown, P. W.: Diverticulitis of the Colon, Surg., Gynec. & Obst. **50**:836-847 (May) 1930.

present, the fecal contents are retained. Mechanical irritation amidst great numbers of micro-organisms results in an inflammatory process, which involves the peridiverticular tissues as well as the diverticulum itself. Marked extension of this process results in tumefaction and stenosis of the lumen of the bowel, with perforation and localized abscess formation as further complications of the original condition. Such abscesses usually do not perforate into the general peritoneal cavity but are well walled off by dense adhesions. Mesosigmoiditis causing the mesentery to be extremely friable is a further complication, which is sometimes not appreciated until surgical attack on the bowel is made. In a small number of patients with perforating diverticulitis the inflamed and perhaps redundant loop of sigmoid flexure will drop low into the pelvis and become either directly or indirectly attached to the bladder. Symptoms of cystitis may be present before actual perforation with establishment of a fistula occurs. The creation of an abnormal channel may or may not be preceded by the formation of an abscess cavity between the sigmoid flexure and the bladder.

Probably the earliest authentic description of a patient with diverticulitis complicated by a sigmoidovesical fistula was reported by Friend.[11] He wrote that his male patient was "seized with a pain, flatus, and a sort of convulsion in his bowels." The patient then passed "pus and gas per urethram for three months." Necropsy showed an inflamed mass of the colon with a hole into the bladder "the size of a goose quill."

Another of the earlier reports of a vesicointestinal fistula which may have been due to diverticulitis is referred to by Morgagni.[12] The reference is given in one of his engagingly communicative letters, the whole of which form one of the fundamental works of modern pathologic anatomy. Discussing an ulceration of the urinary bladder, Morgagni continued:

> . . . and, as in one, the whole bladder is said to have been ulcerated, you will also partly suspect, that an ulcer had reached from thence into some one, or other, of the intestines.
>
> For it might easily happen, that a bladder, in this state, should coalesce with one of the nearest intestines; and that thus a winding sinus might be formed, by means of a kind of ulcerous corrosion, from the one to the other. And in this manner, we may perhaps conceive how the man of whom Young writes, discharg'd, together with a foeculent urine, very small grapes, and particles of leaves, and roots and other things which he had eaten; and with these two pills drawn out into a considerable length.

11. Friend, cited by Wetherell, F. S.: The Diagnosis and Management of Diverticulosis and Diverticulitis of the Pelvic Colon in Women, Am. J. Obst. & Gynec. **35**:417-425 (March) 1938.

12. Morgagni, G. B.: The Seats and Causes of Diseases Investigated by Anatomy, in Five Books Containing a Great Variety of Dissections, with Remarks, to Which Are Added Very Accurate and Copious Indexes of the Principal Things and Names Therein Contained, translated from the Latin by B. Alexander, London, A. Millar & T. Cadell, 1769, vol. 2, p. 541.

It is certain that very severe colic pains had preceded in the former months; so as to make it not altogether improbable, that some inflam'd intestine had coalesc'd with the bladder, and a small abscess being made, that pus had been discharg'd into the cavity of both these viscera, by which a fistula of communication might have been left open betwixt them.

For as to the urine having no disagreeable smell, when Young was call'd to the patient; and as to neither blood, nor pus, being discharg'd in the stools; as to there being no tenesmus; and as to the unctuous fluid, given in the form of a glyster, not having ting'd the urine with its colour; it is true that these circumstances might, with good reason, render it less supposable, with him, that there was a communication betwixt the bladder and the rectum, or betwixt the bladder and the colon.

Another excellent authentic description of a fistula due to diverticulitis with a report of the postmortem examination was that of Jones.[13] A 64 year old woman had passed gas and feces through the urethra. The situation was further complicated by a calculus in the urinary bladder. At postmortem examination about 3 inches (7.6 cm.) of the sigmoid flexure was found to be somewhat contracted. A large number of diverticula were present. Ulceration had occurred at the base of one, allowing the formation of an abscess external to the bowel. The abscess in turn had communicated with the urinary bladder.

In the review of enterovesical fistula by Parham and Hume, the fistula was definitely stated to have been caused by diverticulitis in only 3 cases, while in 65 the cause was classified as inflammatory. No doubt in many cases of the latter group the fistula was caused by diverticulitis. Bryan[14] reported a series of 43 fistulas, and of these 17 were certainly, and 2 were probably, due to this condition. In 18 per cent of Sutton's cases diverticulitis with perforation was the etiologic agent.

Gouverneur, Soupoult and Latifi[15] found 38 fistulas (11 per cent) in 324 cases of diverticulitis of the sigmoid. Higgins collected 328 cases of vesicointestinal fistula and reported that in 160 the fistula was the result of an inflammatory condition. Ninety-two cases of diverticulitis were included in the series. There were 12 cases of fistula in a recent series of 91 cases of diverticulitis in which operation was done by Lockhart-Mummery.[16] Of the 54 sigmoidovesical fistulas described in this presentation, 32, or 59 per cent, were caused by the same pathologic entity.

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13. Jones, S.: Communication Between the Sigmoid Flexure and the Bladder, the Result of Ulceration of a False Diverticulum, Tr. Path. Soc. London **10**:131-132, 1859.

14. Bryan, R. C.: Sigmoidovesical Fistula, with Report of a Case, Ann. Surg. **63**:353-363 (Feb.) 1916.

15. Gouverneur, R.; Soupoult, R., and Latifi, M.: Les fistules colo-vésicales d'origine diverticulaire, J. de chir. **51**:215-231 (Feb.) 1938.

16. Lockhart-Mummery, J. P.: Late Results in Diverticulitis, Lancet **2**:1401-1404 (Dec. 17) 1938.

Most of the patients with diverticulitis complicated by fistula were men (97 per cent), and the average age was 54.8 years. Men are affected in greater numbers because diverticulitis is more frequent in that sex, and an additional fact is that in women the uterus forms an effective barrier between the sigmoid flexure and the bladder. Symptoms referable to disturbance in the urinary bladder were present for periods varying from a few days to many years. There was passage of either gas or feces through the urethra in practically all the cases.

Varying degrees of cystitis were seen through the cystoscope, and visualization of the fistulous opening was possible in 13 of the 30 patients examined cystoscopically. In 9 the aperture was on the left, in 1 it was on the right and in 3 it was in the dome of the bladder. Demonstration of the fistulous tract was possible in only 1 of the 10 cystograms made. Owing to its proximal position, the colonic opening of the fistula to the bladder was seen through the proctoscope in only 1 of the 29 patients subjected to examination. Although the roentgenogram was valuable in demonstrating the regional extent of diverticulitis, the fistulous tract was demonstrable on only one occasion.

The problem of curative treatment of vesicointestinal fistulas in general has brought forth a number of surgical procedures. Barbier de Melle [17] proposed the first rational treatment by suggesting colotomy. Pennel,[18] Curling [19] and Holmes [20] were among the pioneers to employ this operation. Suprapubic cystostomy followed by intravesical closure of the vesical opening was suggested in 1884 by Le Dentu.[21] This method was used by Pousson [22] eleven years later, with temporary success but ultimate failure. Czerny [23] and Boiffin [24] were the earliest champions of an intraperitoneal approach to surgical correction of the fistula.

A true evaluation of the surgical methods used in the treatment of sigmoidovesical fistula due to diverticulitis is difficult to attain, since

17. Barbier de Melle, cited by Chavannaz, G.: Des fistules vésico-intestinales acquises chez l'homme, Ann. d. mal. d. org. génito-urin. **15**:1176-1199, 1897; **16**: 203-217, 1898.

18. Pennel, C.: A Case of Stricture of the Rectum, Wherein an Artificial Anus Was Established in the Left Lumbar Region, with Remarks, Lancet **1**:628, 1850.

19. Curling, cited by Parham and Hume.[1]

20. Holmes, T.: A Case of Lumbar Colotomy (Amussat's Operation) Successfully Performed for the Relief of Vesico-Intestinal Fistula, Lancet **1**:400-401 (April 14) 1866.

21. Le Dentu, cited by Parham and Hume.[1]

22. Pousson, cited by Parham and Hume.[1]

23. Czerny, cited by Parham and Hume.[1]

24. Boiffin: Rétrécissement du côlon ascendant, abcès couvert dans le rectum et la vessie: Entéroanastomose, Bull. et mém. Soc. d. chir. de Paris **17**:305-309 (April) 1891.

the majority of case reports are deficient as to details of the procedure used. In addition, the actual number of patients with diverticulitis suffering this unfortunate complication is small. A large series must be accumulated before adequate judgment as to the true value of any single procedure can be formed. With a small group, if end results are expressed on a percentage basis a false conception as to efficacy of treatment and mortality may be entertained. If only 3 patients in the whole series are subjected to one procedure and 1 succumbs, the mortality thus stated would be 33.3 per cent. However, the same operation employed on 3 other patients might result in three cures. Therefore, the expression of results by the percentage system will be avoided here, and only actual statistics will be presented.

A survey of the existing literature yields a number of methods used in the surgical attack on fistula due to diverticulitis. The three chief avenues of approach are: (1) colostomy or cecostomy alone, (2) a single stage procedure with or without the establishment of an artificial abdominal anus and (3) a multiple stage operation. Diversion of the fecal current and subsequent surgical treatment of the fistulous tract and adjoining regions by varied methods are the main components of the multiple stage operation. Included among such methods are (1) excision of the tract with simple closure of the sigmoidal and vesical openings, (2) closure of the aperture in the bladder combined with a Paul-Mikulicz procedure on the involved portion of the sigmoid flexure and (3) suture of the vesical opening and resection, with end to end anastomosis of the diseased sigmoid flexure. Surgical mortality attendant on such procedures as a whole is markedly elevated but varies considerably between individual approaches.

Simple colostomy as close as is practicable to the site of the lesion is the simplest way of handling the problem, and, as would be expected, the primary mortality rate from such a procedure is low. At this point, it is well to keep in mind that when colostomy is performed it should be designed with the purpose of preventing spilling from the upper barrel into the lower barrel. If sufficient time is allowed to elapse, often the fistula will close spontaneously if the fecal current has been well diverted. If the colonic stoma is not placed as close as is feasible to the inflammatory mass, a large amount of inspissated material may collect in a redundant loop of bowel between the colonic stoma and the region of inflammation. This should be avoided if possible. Cecostomy should be employed, perhaps, only if marked obstruction is present and then as a preliminary to colostomy.

Two patients of the present group have been reported on previously, and their cases have been reviewed by Kellogg. When these are deducted from his series, there are left 28 cases of fistula due to diverticulitis and 7 of fistula probably due to it. Thirteen patients in all were sub-

jected to colostomy, and 11 were cured. One remained unimproved, and 1 died. This last figure is of great importance.

One stage procedures were performed in 12 cases of Kellogg's series. These included (1) primary separation and suture of the bladder and intestine; (2) primary separation, repair of the bladder, resection of the bowel and end to end anastomosis; (3) the first procedure described, with the addition of a permanent colostomy; (4) the same procedure, except that a cecal stoma was established instead of a vent in the more distal portion of the colon; (5) primary separation of the bowel, repair of the bladder, resection of the bowel with end to end anastomosis and cecostomy, and (6) primary separation, repair of the bladder, resection of the sigmoid flexure (method not stated) and permanent colostomy. With the first procedure, 2 patients were cured and 1 died; with the second, 2 were cured; with the third, 1 was cured; with the fourth, 2 died; with the fifth, 1 was cured, and with the sixth, 2 were cured and 1 died.

Four patients were subjected to a multiple stage operation. An artificial abdominal anus was made in some portion of the colon proximal to the lesion, and at a subsequent date separation and suture of the sigmoid flexure and urinary bladder were done. The abdominal vent was made permanent in only 1 case. All of these patients were cured.

Of the 17 patients in this group on whom colostomy was performed either as a total therapeutic procedure or as a preliminary to secondary operations, only 1 died. The results were good also in the group treated with resection secondary to colostomy, in which there were no deaths attributable to the latter procedure.

To arrive at a more complete evaluation of the surgical procedures used in the present series of fistula due to diverticulitis, 6 cases previously reported by Sutton are added. Multiple modes of treatment were used in these 38 cases, inasmuch as the procedures were performed by a number of different surgeons over a period of thirty-two years.

On 8 patients of this group colostomy alone was performed, without primary operative mortality. Likewise, there were no deaths in an additional group of 11 patients in whom an abdominal fecal vent was made preparatory to subsequent operations. One of the patients in the latter group was operated on elsewhere.

A primary attack on the fistula itself, varying in detail, was used in 16 cases. In the largest proportion (8 cases) there were performed primary separation of the involved parts and suture of the bladder and intestine. There was 1 recurrence, one year after the operation. Three postoperative deaths from peritonitis resulted. Transverse colostomy was performed in an additional case in which there had been the same primary attack on the fistula. Closure of the aperture in the bladder and exteriorization of the affected bowel as a Paul-Mikulicz operation

was performed in 5 cases, with 2 "primary" deaths. The vesical opening was sutured and resection with end to end anastomosis over a rubber tube was done in another case, with a favorable result. The last-mentioned type of procedure with the addition of appendectomy was performed in an additional case, with resulting cure. In the group as a whole there were 5 deaths directly attributable to the surgical procedure.

Diversion of the fecal stream from its natural channel and a secondary approach to the fistula were made in 12 cases. Second stage procedures were performed at periods varying from about three weeks to five years and five months. Resection of the involved portion of bowel by the Paul-Mikulicz operation was employed in 4 instances, resection with end to end anastomosis in 5 instances and separation and simple closure of the openings in 2. In 1 case anterior resection was performed, but the distal end of the bowel was closed and dropped back into the pelvis. Two of the patients subjected to each of the first two procedures and the 1 subjected to the last procedure died. However, of the 5 deaths, 3 were but indirectly due to the surgical procedure. Evisceration followed by peritonitis was responsible for the death of 1 of the patients whose sigmoid flexure had been exteriorized; a hemorrhage on the twenty-fifth postoperative day accounted for the death of another patient, in whom a primary anastomosis had been made, and a third died of a fatal pulmonary embolus.

The length of the interval between operations depends on the general condition of the patient and the reaction of the fistula to the passage of time. Certainly the interval should be at least six months to one year to allow spontaneous closure of the fistula. In this particular study the lapse of a longer period seemed to have no effect on mortality.

In 2 other patients in this group with diverticulitis primary separation of the involved viscera and repair of the openings were performed. However, a recurrence of symptoms in both necessitated further surgical procedures. In 1 the vesical opening was again closed and the involved portion of the sigmoid flexure exteriorized, with resulting cure. Intravesical closure of the fistulous tract and establishment of a colonic stoma above the site of the lesion resulted in improvement in the other patient. However, he succumbed to an unrelated illness while at the clinic, so that a true evaluation of the end result could not be obtained.

Computation of results reveals cures in 15 cases and 10 "primary postoperative" deaths. Two additional patients secured excellent results from operation but unfortunately had a persistent fecal fistula at the site of colostomy. Recurrences took place in 2 patients seven and nine years respectively after operation. One patient had undergone primary separation of the sigmoid flexure and the bladder with closure of the

openings; on the second a colostomy had been performed, with later closure of the openings as has been described. The colonic stoma was subsequently closed.

Several interesting facts are presented in connection with the group of patients on whom colostomy was performed as the sole surgical procedure. Three patients had no relief from the operation, but further surgical intervention was prohibited in 1 by age and poor general condition. When last seen, 1 patient had improved to such an extent that he was to return for a resection of the sigmoid flexure. Two other patients obtained excellent results from colostomy, but when the abdominal colonic stomas were closed recurrence of symptoms referable to the fistula took place. The closure in 1 of these patients broke down, and a fecal fistula resulted. Colostomy was again performed elsewhere in the other patient in whom recurrence was noted, and he subsequently succumbed to an operation of unknown character, presumably on the sigmoid flexure. Death from an unrelated cause claimed an additional patient in this group. The reason for the death of the last patient could not be ascertained.

The procedure of choice for any given patient cannot, of course, be postulated. Any number of conditioning factors must affect the surgeon's choice. Age, general physical status, amount and degree of involvement of the affected bowel, the exact location of the inflamed region and the condition of the mesentery are but a few of the necessary factors demanding evaluation before decision as to a definite operation is made. A friable mesentery and bowel will make suturing difficult, as the sutures will pull out easily. Infection will be spread more easily, notwithstanding meticulous technic. When the region of diverticulitis is proximal in the sigmoid flexure, exteriorization may be carried out; resection with end to end anastomosis may be necessary in the more distal portion. A slight amount of inflammation may permit primary separation of the adherent structures and suture of the openings.

However, the lessons learned in surgical treatment of the bowel for other conditions are readily applicable to diverticulitis with fistula, for the same general principles hold. It would seem, therefore, that any conservative approach to cure should include a preliminary colostomy close to the site of the lesion. Furthermore, such a vent should be absolute, so that fecal material will not go over the spur and eventually reach the diseased bowel. If the symptoms subside and the fistula closes spontaneously, the colonic stoma may be subsequently closed. This operation, however, should be performed only if a sufficient interval has elapsed to allow complete subsidence of the inflammatory process in the sigmoid flexure. This must be checked by proctoscopic and roentgen studies in addition to thorough consideration of the patient's course after colostomy had been performed. Occasionally, however, one

observes a favorable result from colostomy, with subsidence of the diverticulitis and closure of the fistula, but when the abdominal colonic stoma is closed, symptoms referable to the sigmoidovesical fistula are again present. In such a case, resection of the involved portion of bowel after preliminary colostomy will have to be done if cure is to be effected.

If resection of the sigmoid is decided on after a sufficient interval, the type of operation used should depend to some extent on the exact location of the lesion in the sigmoid flexure. Whenever possible, a Paul-Mikulicz operation is the procedure of choice for the upper part of the sigmoid flexure. Occasionally a lesion distal in the bowel may be exteriorized by opening the pelvic peritoneum and freeing the colon. If this is not possible, resection and end to end anastomosis may be necessary.

Free drainage of the urinary bladder is essential and may be achieved by either a suprapubic tube or an indwelling urethral catheter. The latter also offers a means of irrigating the bladder.

It may be well at this point to quote from no less eminent an authority than Harrison Cripps,[25] who wrote in 1888: "The idea of abdominal section with a view to separating the intestine from the adherent bladder and closing the openings might at first be thought possible, but after investigating museum specimens and the accounts of postmortem examinations, the proceeding, I fear, will be seldom practicable."

Carcinoma of the sigmoid flexure was responsible for the fistula in 12 patients. Differentiation of a malignant lesion from a region of diverticulitis may be extremely difficult at times. The average age of these patients was 49.7 years, and all except 2 were men. The symptoms in general were similar to those encountered in the group with diverticulitis. Proctoscopic examination, roentgen studies of the colon and cystoscopic examination were useful adjuncts in establishing the diagnosis.

Particular attention should be called to 2 patients who presented on primary cystoscopic investigation large tumor masses in the bladder. If the entire situation is not carefully reviewed, an error in diagnosis may be made. Vesicosigmoidal fistula due to primary carcinoma in the urinary bladder is extremely rare, and the lower part of the colon should be thoroughly investigated in all cases in which the fistula is thought to be due to a neoplasm of the bladder.

Invasion of the wall of the bladder by a malignant growth of the sigmoid flexure engenders an extremely poor prognosis. However, if metastases are not demonstrable operation should be undertaken. The type of operation depends on the particular skill of the surgeon and the exact situation of the growth. In any event, the involved portion

25. Cripps, H.: Passage of Gas and Feces Through the Urethra: Colotomy; Recovery; Remarks, Lancet **2**:619-620 (Sept. 29) 1888.

of the bladder must be resected and the bladder closed. Suprapubic cystostomy may be performed or the bladder drained with an indwelling catheter. Of the 12 patients, 11 succumbed either immediately after the operation or shortly thereafter. The fate of the other patient in this group is unknown, but he had an inoperable lesion at the time of operation, so that a palliative colostomy was performed.

In the group with sigmoidovesical fistula there were 9 patients whose fistula was due to an inflammatory condition which was not diverticulitis and 1 with an inflammatory condition which might have been diverticulitis. Six of these patients were women, and 4 were men. The average age of the entire group was 42.8 years. Six were simply classified as having an inflammatory condition, 1 as having an inflammatory condition and a questionable malignant lesion and 2 as having tuberculosis. Seven of the patients in this group had undergone an abdominal operation elsewhere previously, the fistula being the result of infection following operation. One of the patients had had a tuberculous ovary removed here, and a sigmoidovesical fistula had developed postoperatively. The symptoms referable to the fistula were the same for the whole group as have been described previously.

As would be expected, surgical approach to the group of inflammatory lesions was most difficult. The intestines are usually adherent to one another and the surrounding structures, making any procedure hazardous. In addition, the patients usually have been ill for prolonged periods and have lost considerable weight and strength. Primary separation of the sigmoid flexure and the bladder with suture of the apertures was employed in 5 patients. One was completely cured, and in 2 a fecal fistula developed postoperatively, with, however, complete relief of vesical symptoms. The other 2 patients died. Even such simple procedures as colostomy and ileostomy were attended with poor results. Colostomy afforded complete relief of symptoms referable to the urinary tract in 1 patient, while another died at home of an unknown cause two months after operation. The patient subjected to ileostomy had fistulas involving the ileum, the sigmoid flexure and the bladder, and she succumbed at home postoperatively.

Primary repair and closure of the fistula were done on 1 of the patients with tuberculosis, and an excellent result was obtained. The second of these patients had been operated on elsewhere for the same condition, and although multiple procedures were employed here, he remained unimproved.

Postmortem studies were conducted on 11 patients in the entire series. The causes of death and the state of the kidneys are difficult to determine in the cases in the literature. Peritonitis accounted for the deaths of 7 of the 11 patients; 2 succumbed to bronchopneumonia,

1 to a hemorrhage on the twenty-fifth postoperative day and 1 to surgical shock. The kidneys were normal in 5 patients. Pyelonephritis was present in 2 patients; the renal pelves were dilated in 1, and a fourth had a combination of dilated pelves and enlarged kidneys. The latter condition alone was found in 2 patients.

Table 2 is a summary of results in the series reported by Sutton and in the present group.

The mortality demands some explanation. Included among these patients are those who had extensive carcinoma of the sigmoid flexure with involvement of the bladder and in whom it was deemed expedient to perform radical resection. The prognosis is extremely poor in such cases. Also included in this group are those patients who were subjected to secondary operations necessary for the alleviation of rather severe inflammatory conditions of the abdomen. Very important is the fact that most of these patients were in the fifth, the sixth and even

TABLE 2.—*End Results in Eighty-Eight Cases of Surgically Treated Sigmoidovesical Fistula*

Cured	35
Sigmoidovesical fistula cured, but fecal fistula remained	7
Improved	5
Unimproved	4
Recurrence	4
Deaths	
Attributable to primary disease or operation for correction	26
Attributable to unrelated cause	1
Attributable to unknown cause	2
End result unknown	4

the seventh decade of life. The mortality from any operation in the period between 50 and 70 years of age is considerably enhanced, and procedures for the cure of sigmoidovesical fistula are no exception. However, the plight of this unfortunate group of persons is so miserable that one is forced to heroic measures to alleviate their distress.

CONCLUSIONS

1. Diverticulitis with perforation is perhaps the leading factor in the production of sigmoidovesical fistula.

2. The formation of a fistula is an extremely serious complication in patients with diverticulitis or other inflammatory conditions.

3. The mortality from one stage surgical procedures for correction of fistula due to diverticulitis is excessive.

4. With the facts learned from other surgical procedures on the bowel in mind, multiple stage operations are most satisfactory in dealing with this particular type of fistula. Colostomy which obviates spilling

from the upper into the lower part of the colon is usually the first stage, and it should be performed as close to the fistula as is practicable, to avoid redundant bowel above the vesicocolonic tract.

5. A sufficient interval should be permitted to elapse after preliminary colostomy to allow spontaneous healing of the fistula to occur if it will. If it does occur, the colonic stoma should not be closed until one is positive that the inflammation in the sigmoid flexure has completely subsided; otherwise there will be a recurrence.

6. When carcinomatous invasion from the sigmoid flexure of the colon into the bladder has occurred and a sigmoidovesical fistula has formed, the prognosis is extremely poor.

7. Ascending infections of the urinary tract are not common complications of vesicosigmoidal fistula.

CLINICAL USE OF A SYNTHETIC SUBSTANCE RESEMBLING VITAMIN K (2-METHYL-1, 4-NAPHTHOQUINONE)

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In 1939, McKee and Doisy and their co-workers [1] showed that vitamin K has a quinoid structure. This led to investigation of the antihemorrhagic value in cases of experimental hypoprothrombinemia of many of the quinones. Of those examined, the 2-methyl-1,4-naphthoquinone and the 2-methyl-3-hydroxy-1,4-naphthoquinone possessed the greatest antihemorrhagic activity.[2] Rhoads and Fliegelman [3] have recently reported favorable results in the control of hypoprothrombinemia in the human patient by the use of 2-methyl-1,4-naphthoquinone. Binkley, Doisy and others [4] and Feiser [5] have recently shown that 2-methyl-3-phytyl-1,4-naphthoquinone and the natural vitamin K possess identical physical properties and the same empiric formula.

PRESENTATION OF DATA

In this paper are presented 10 cases of clinical hypoprothrombinemia of various causes and the responses of the patients to administration of

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1. McKee, R. W.; Binkley, S. B.; MacCorquodale, D. W.; Thayer, S. A., and Doisy, E. A.: The Isolation of Vitamins K_1 and K_2, J. Am. Chem. Soc. **61**: 1295 (May) 1939.

2. (*a*) Ansbacher, S., and Fernholz, E.: Simple Compounds with Vitamin K Activity, J. Am. Chem. Soc. **61**:1924 (July) 1939. (*b*) Almquist, H. J., and Klose, A. A.: The Anti-Hemorrhagic Activity of Certain Naphthoquinones, ibid. **61**:1923 (July) 1939. (*c*) Thayer, S. A.; Cheney, L. C.; Binkley, S. B.; MacCorquodale, D. W., and Doisy, E. A.: Vitamin K Activity of Some Quinones, ibid. **61**:1932 (July) 1939.

3. Rhoads, J. E., and Fliegelman, M. T.: The Use of 2-Methyl-1,4-Naphthoquinone in the Treatment of Prothrombin Deficiency in Patients, J. A. M. A. **114**:400-401 (Feb. 3) 1940.

4. Binkley, S. B.; Cheney, L. C.; Holcomb, W. F.; McKee, R. W.; Thayer, S. A.; MacCorquodale, D. W., and Doisy, E. A.: The Constitution and Synthesis of Vitamin K_1, J. Am. Chem. Soc. **61**:2558 (Aug.) 1939.

5. Feiser, L. F.: Identity of Synthetic 2-Methyl-3-Phytyl-1,4-Naphthoquinone and Vitamin K_1, J. Am. Chem. Soc. **61**:2561 (Aug.) 1939.

2-methyl-1,4-naphthoquinone. These cases are summarized in the accompanying table. Daily studies of the plasma prothrombin were made for each patient while he was receiving the drug. The prothrombin times were determined at 37 C., a modification of Quick's method being used and the prothrombin time of normal human plasma being employed as the standard. In all cases the value for plasma fibrinogen was normal. Each patient was given 0.325 Gm. of bile salts with each 2 mg. of

Summary of Ten Cases

Case	Diagnosis	Prothrombin Time (Per Cent of Normal)			Treatment		Comment
		Before Therapy	24 Hrs. After Therapy Began	End of Therapy	Total Amount, Mg.	Number Days Treated	
1	Stricture of common duct	15	100	100	40	5	Bleeding gums and menorrhagia; both ceased within 8 hours after beginning treatment
2	Common duct stone	65	100	100	32	4	
3	Carcinoma of head of pancreas	75	100	100	24	3	
4	Obstructive jaundice from adhesive band across common duct	83	100	100	24	3	
5	Biliary fistula.....	54	100	100	32	3	
6	Nontropical sprue...	24	32	100	128	16	Normal prothrombin time not obtained until the 16th day
7	Hepatitis.....	60	50	100	60	5	Vomited and did not retain vitamin K; 48 hours after I.V. vitamin K, prothrombin time was normal
8	Acute yellow atrophy	28	33	66	48	6	Died on 8th day, in coma
9	Cirrhosis.....	50	50	38	140	14	Bile in stools
10	Cirrhosis.....	28	32	38	40	5	Bile in stools

2-methyl-1,4-naphthoquinone except those in cases 7 and 9, who also received a water-soluble sulfonated derivative of this naphthoquinone.[6]

The typical response to this naphthoquinone is graphically illustrated in chart 1 (case 1). The patient was bleeding from the gingival margins and had many cutaneous ecchymoses associated with obstructive jaundice. Eight hours after the first administration of this drug the bleeding ceased and no more ecchymoses appeared. In chart 2 (case 9) is shown the failure of this substance to increase a reduced level of plasma prothrombin in a case of advanced cirrhosis of the liver. As will be

6. The oral preparation of 2-methyl-1,4-naphthoquinone and the bile salts (bilron) were supplied by Eli Lilly & Co. The sulfonated water-soluble preparation was supplied by the Abbott Pharmaceutical Laboratories.

noted in the chart, daily oral doses of this substance failed to improve the prothrombin time. On the thirteenth day of treatment the intravenous route was substituted, 12 mg. of the aqueous-soluble substance being given without effect.

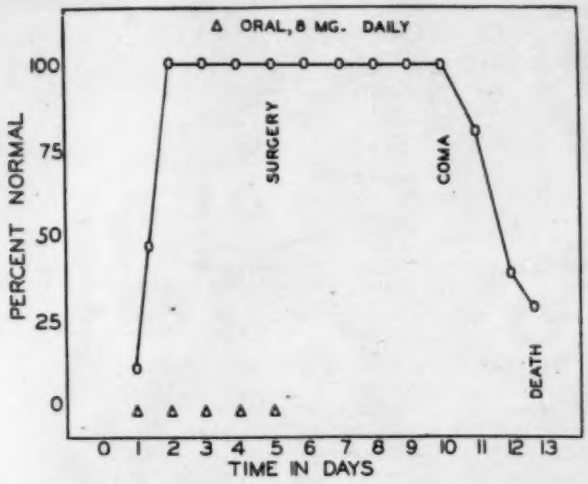
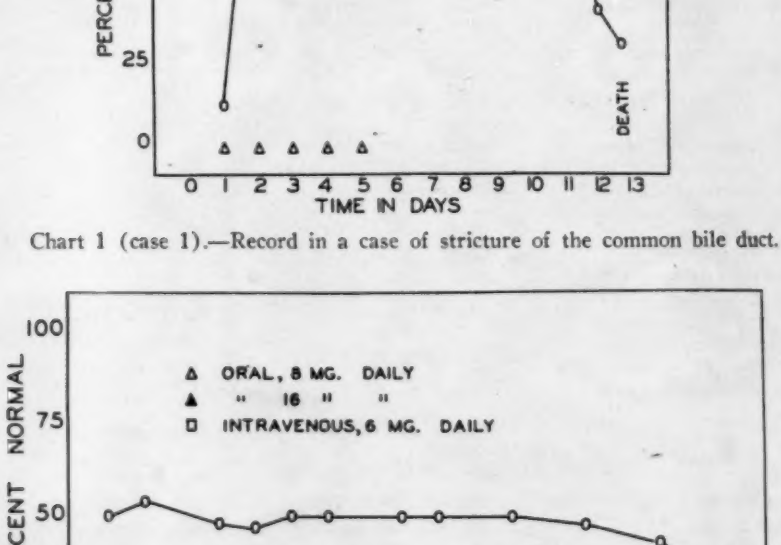


Chart 1 (case 1).—Record in a case of stricture of the common bile duct.


Δ ORAL, 8 MG. DAILY
▲ " 16 " "
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PERCENT NORMAL
100
75
50
25
0
Δ Δ Δ Δ Δ Δ Δ Δ ▲ ▲ ▲ ▲ □ □
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
TIME IN DAYS

Chart 2 (case 9).—Record in a case of cirrhosis of the liver.

COMMENT

These cases present three types of response to the naphthoquinone. The first is that seen in cases 1, 2, 3, 4 and 5, in which the prothrombin rapidly returned to normal levels. In each of these cases the low level

of plasma prothrombin was produced by defective absorption of vitamin K, attributable to the absence of bile in the intestinal tract. When this absorption defect was corrected by oral administration of bile salts, the prothrombin rapidly returned to normal when the naphthoquinone was given.

The low level of plasma prothrombin in the patient with nontropical sprue (case 6) is a manifestation of inadequate absorption of vitamin K together with other fat-soluble substances. The sluggish type of response seen in this case might have been expected, since the concentration of the vitamin in the intestinal tract was increased without any change in the fundamental absorption defect. In two previous studies on this patient similar responses were observed when the alfalfa concentrate was given.

In cases 9 and 10 no appreciable change in the prothrombin time was produced by the naphthoquinone. The patients in both of these cases had far advanced cirrhosis of the liver associated with chronic alcoholism. Bile salts were given with the 2-methyl-1, 4-naphthoquinone, although adequate bile was already present in the stools of both patients. In case 9, after twelve days of therapy, during which time 128 mg. of the naphthoquinone was given orally, the water-soluble sulfonated derivative of the naphthoquinone was given in two doses of 6 mg. each by vein. This assured the presence of the preparation in the circulation, but even under these conditions the prothrombin time did not improve. The failure of the plasma to respond in these cases suggests that in the presence of advanced hepatic cirrhosis the process of activation of prothrombin by the naphthoquinone may be impaired.

None of the patients studied showed any symptoms of untoward reaction or toxic symptoms which might be ascribed to this drug. All patients received at least 8 mg. of this substance daily, while those in cases 7 and 9 received as much as 16 mg. daily for two and four days respectively. The patient in case 9 received a total of 140 mg. of naphthoquinone over a sixteen-day period, without ill effects. Occasional nausea was observed, but this was not present if the bile salts were omitted in a test dose. However, until further clinical data are at hand the naphthoquinones should not be used unless the patient can be carefully observed.

The results obtained with naphthoquinone in these patients compare favorably with the results obtained in this clinic in prothrombin-deficient patients receiving the vitamin K concentrate. However, there is considerable variance of opinion as to the relative antihemorrhagic values of the alfalfa concentrate and the synthetic naphthoquinones in the case of the experimental animal. It is generally agreed that the 2-methyl-1, 4-naphthoquinone and the 2-methyl-3-hydroxy-1, 4-naphthoquinone have a high degree of activity, the former possessing more activity than the latter. Ansbacher and Fernholz [2a] stated the belief that the 2-methyl-1,

4-naphthoquinone is as active as the natural vitamin, while Almquist and Klose [2b] stated that this synthetic preparation is considerably less potent than the concentrate. However, until it is possible to assay pure natural vitamin K in terms of its naphthoquinone content, no accurate comparisons can be made between this natural vitamin and the synthetic preparations.

SUMMARY

Ten patients with low levels of plasma prothrombin were given synthetic 2-methyl-1,4-naphthoquinone, and their responses were recorded.

The failure of prothrombin response in 2 cases of advanced cirrhosis of the liver is discussed.

No evidence of toxicity was observed during administration of this substance.

Dr. Lester R. Dragstedt gave helpful advice and valuable criticism in the preparation of this paper.

REGIONAL AND GENERAL TEMPERATURE RESPONSE FOLLOWING EXPERIMENTALLY INDUCED ACUTE INFLAMMATION AND INFECTION

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In the course of experimental work on surgical infections it seemed necessary to study anew the temperature responses of the body to acute inflammations and infections. For our own purposes it was desirable to observe the relation between the deep temperatures of the brain, liver, rectum and muscles in the normal subject; the variations in deep temperature as influenced by the commonly used anesthetic drugs; the time of appearance of elevation of temperature in the tissues involved and in the intra-abdominal organs and the brain after production of an acute localized inflammation; the reliability of the rectal temperature as a guide to the febrile state of the subject, and the relation between leukocytic response and elevation of temperature. Observations of this sort have, of course, repeatedly been made, but such observations and their interpretations as published in the literature have varied greatly. As a preliminary study it appeared desirable to become familiar with and to standardize the methods available to us and to make certain observations of our own under conditions obtained in our laboratory. The preliminary observations are reported here.

APPARATUS AND METHODS OF OBSERVATION

The particular assembly used in the experiments herein reported was one having a portable potentiometric temperature indicator,[1] five needle style thermocouples and a rotary thermocouple switch. The temperature range for the assembly was from —4 to 50 C. The thermocouples [2] were made from no. 20 Stubbs gage needles of platinum-iridium shafts and bakelite handles with no. 14 iron-constantan duplex lead wires. These thermocouples can be sterilized by boiling in water. The assembly was so arranged that it was possible to take temperature readings at five

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1. No. 8663, Leeds and Northrup Company, Philadelphia.

2. These thermocouples were constructed by the Leeds and Northrup Company, Philadelphia.

different parts of the body of the experimental animal within one minute. This apparatus has an estimated accuracy within 0.005 degree (C.).

Dogs were used in these experiments. For observations of the temperature of the brain, the animals were prepared by preliminary trephine of the temporal bone, the opening being uniformly placed over the midparietal region of the cerebral cortex. For observations of the temperature of the liver, a preliminary operation was done; a rib over the right lower lateral aspect of the thorax was resected, and the costophrenic sulcus was obliterated by suturing the diaphragmatic to the parietal pleura. Animals were not used for experimentation until seven days after the operation, at which time the wounds were healed. The needle style thermocouples were inserted to a depth of 2 cm. into the subcortical substance of the brain and held securely in place by means of a rubber flange fastened to the scalp with adhesive tape. The couples were inserted into the substance of the liver to a depth of 5 cm. and anchored in the same fashion. The rectal temperature readings were made by inserting a thermocouple into the ampulla of the rectum for a distance of 5 cm. The temperatures of the muscles were determined by inserting a thermocouple for a distance of 5 cm. obliquely into the muscles of the thigh on the outer aspect of the leg. Readings were made at all points every two, five or ten minutes, according to the plan of the experiment. The thermocouples were regularly checked with a series of finely graded mercury thermometers. The temperature of the room was not allowed to vary over 3 degrees (C.), and wind currents were excluded. The humidity of the room was recorded in volumes per cent by polymeter (Lambrecht's). During the experiments, many of which were carried on for twenty-four hours, no attempt was made to supply nourishment to the experimental animal or to replace the loss of fluid from the body.

NARCOSIS AND ANESTHESIA

In experiments 1 to 5, observations were made on deep temperatures in dogs after morphine medication and the use of certain anesthetic drugs. All experiments were of two hours' duration. Thermocouples were inserted in the liver, the rectum and (in experiment 5) the brain. Readings were made every two minutes. The room temperature was 25 to 26 C. The humidity was 35 to 40 volumes per cent.

EXPERIMENT 1.—A dog weighing 11.6 Kg. was given 0.01 Gm. of morphine intramuscularly. Anesthesia was not used. At the beginning of the experiment the temperature of the liver and that of the rectum were the same, but the former quickly fell below the latter, and this relation between the two temperatures persisted. Both showed a gradual decrease. Twenty-four minutes after the start of the experiment the temperature of the liver reached a constant of 37.2 C.; the rectal temperature continued to drop and did not reach a constant until forty-eight minutes had elapsed. From this point the two temperatures were within 0.5 degree (C.) of each other. Ice applied to the head for eleven minutes was not followed by a demonstrable change in the temperature of either the rectum or the liver. Ice compresses applied to the abdomen for twenty-one minutes caused a rapid drop of 0.7 degree (C.) in the temperature of the liver. The temperature of the rectum did not fall until four minutes later and dropped only 0.5 degree (C.). After removal of the cold application both temperatures rose; the temperature of the rectum returned to 37 C., and that of the liver rose to 36.8 C. toward the end of the experiment.

EXPERIMENT 2 (*Amytal Sleep*).—A dog weighing 12 Kg. was given 1.1 Gm. of amytal intraperitoneally. Fifteen minutes afterward the temperature of the liver and that of the rectum were approximately equal, at 38.6 C. Both began to fall immediately, that of the liver more rapidly than that of the rectum. The fall continued for thirty minutes, after which both values became fairly constant. Throughout the remainder of the two hours both remained constant, that of the liver at 37.8 C. and that of the rectum at 37.9 to 37.95 C.

EXPERIMENT 3 (*Spinal Anesthesia*).—A dog weighing 13 Kg. was anesthetized with 50 mg. of procaine hydrochloride given into the subarachnoid space at the level of the second lumbar vertebra. Immediate paralysis of both hindlegs resulted. The first temperature observation was taken three minutes after the onset of paralysis of the hindlegs. The temperature was 39.5 C. (temperature before anesthesia, 37.4 C.). It rose rapidly to a peak at 40.2 C. and dropped slowly after thirty minutes. As the effect of the anesthetic wore off, the rectal temperature reached a "low" of 39.2 C., at which point the experiment was abandoned because of muscular activity of the lower extremities of the animal.

EXPERIMENT 4 (*Avertin Anesthesia*).—A dog weighing 13.6 Kg. was anesthetized with 80 mg. of avertin in amylene hydrate per kilogram of body weight, administered by rectum. The rectal temperature was observed to hold a slightly higher level than that of the liver throughout. The temperature of the rectum was 38 C. at first and fell gradually to 37.8 C. That of the liver was 37.9 C. and fell gradually to 37.6 C.

EXPERIMENT 5 (*Amytal Sleep*).—A dog weighing 13.6 Kg. was given 0.8 Gm. of amytal intraperitoneally. The temperatures of the liver, brain and rectum stayed between 37.5 and 39 C., and all these were closely parallel as they slowly dropped through the two hours. The deep cerebral temperature was highest, the temperature of the liver was intermediate and the rectal temperature was lowest.

INFLAMMATION

In experiments 6 to 10, observations were made on the deep temperatures and on the leukocytic reaction in dogs after production of a localized acute aseptic inflammation by means of sterilized turpentine-paraffin solution. All except experiment 10 were of twenty-four hours' duration, readings being taken every ten minutes. Thermocouples were inserted in the brain, the liver, the rectum and the muscles of the thighs. The room temperatures ranged from 24 to 28 C. The humidity was from 25 to 35 volumes per cent.

EXPERIMENT 6.—A dog weighing 12 Kg. was given 1.1 Gm. of amytal intraperitoneally. The temperatures of the liver, rectum and brain underwent similar variations, but their relation to each other was not constant. At the start of the experiment the rectal temperature was 38.8 C. At this level it was slightly higher than that of the brain or the liver. However, after three hours the temperature of the liver became highest and remained so throughout the twenty-four hour period. Up to twelve hours there was a gradual rise in all three deep temperatures, this rise giving to the curves a sloping apex, followed in the second twelve hours by a decline to meet, approximately, the readings recorded at the start of the period. The temperature of the muscles of the left leg was higher at the start (34.5 C.) than that of the right leg. This relation reversed itself several times as the

experiment progressed. The leukocyte count, starting at 19,500 per cubic millimeter, rose irregularly to 23,000 at the end of nineteen hours, then dropped to 20,000. The maximal leukocytosis occurred later than did the maximal rise in deep temperatures of the liver, rectum and brain. This experiment was planned as a control for experiments 7 to 10.

EXPERIMENT 7.—A dog weighing 11 Kg. was given 0.74 Gm. of amytal intraperitoneally. In this experiment a localized inflammatory process was initiated in the muscles of the right thigh by the injection of 6 cc. of a turpentine-paraffin solution (prepared by heating a mixture of 2 parts paraffin and 1 part turpentine, by volume), which had been sterilized and cooled to 30.5 C., into the area where the thermocouple was inserted into the tissue. The injection was followed by a rise in muscular temperature of over 7 degrees (C.). This rise manifested itself uninterruptedly in the course of four hours, rapidly at first, then less rapidly. Associated with the rise in peripheral temperature there was a sharp elevation of the temperatures of the liver, rectum and brain and an increase in the leukocyte count from 7,000 to 25,000 per cubic millimeter. As the temperature of the peripheral area dropped through the next twenty hours to reach the approximate level at which readings had been made before the injection, the tissue temperatures in the liver, the rectum and the brain continued to ascend, and the leukocyte count remained elevated.

EXPERIMENT 8.—A dog weighing 12.4 Kg. was given 0.74 Gm. of amytal intrapenitoneally. In this experiment a localized inflammatory process was initiated in the muscles of the left thigh by injection of 6 cc. of turpentine-paraffin solution, sterilized and cooled to 35 C., approximately at the point where the thermocouple had been inserted. There was a rapid rise in temperature of the muscles of the thigh; the rise was only 2 degrees (C.), but the level to which it brought the temperature was the same as in experiment 7 (37 C.). The temperatures of the intracranial and intra-abdominal organs showed a gradual and steady elevation.

In the last twelve hours of this experiment the temperature of the inflamed area (musculature of the left thigh) remained elevated and did not drop as it did in the same period in the preceding experiment. Again the relation of the temperatures of the liver, rectum and brain to each other was unaffected by the peripheral inflammatory process.

EXPERIMENT 9.—A dog weighing 11.8 Kg. was given 0.74 Gm. of amytal intraperitoneally. In this experiment 6 cc. of a turpentine-paraffin solution (sterilized and cooled to 37 C.) was injected into the musculature of the right thigh. The behavior of the temperatures of the tissues of the leg was roughly similar to that observed in experiments 7 and 8. The affected leg showed a rise in temperature following the injection, which was maintained persistently throughout the twenty-four hour period at a point averaging 1.5 degrees (C.) above that of the unaffected extremity. The temperatures of the intracranial and intra-abdominal organs again exhibited a persistent elevation. The leukocyte count, which rose from 11,000 to 16,800 per cubic millimeter, exhibited a curve which closely paralleled that shown in experiment 7.

EXPERIMENT 10.—A dog weighing 17.5 Kg. was given 1.1 Gm. of amytal intraperitoneally. When the temperatures of the tissues had reached a fairly constant level (one hour after the observations were started), the dog was placed in an especially constructed cabinet which covered the body from the upper part of the abdomen down to and including the feet. The cabinet was made of wood, its sides having glass windows for observation. The extensions of the couples passed through rubber-stoppered openings in the sides of the cabinet. The cabinet was

heated by incandescent bulbs. The temperature within the cabinet was purposely maintained at a higher level than any of the peripheral temperatures observed in the previous experiments, an attempt being made to determine whether the temperature of an inflamed area might rise above that of the environment. After the animal was placed in the cabinet, all the tissue temperatures rose. Aften one hour and twenty minutes an inflammatory process was initiated in the tissues of the right thigh by injection of a mixture of turpentine and paraffin, prepared as in the earlier experiments. The temperatures of the brain, liver and rectum did not exceed that of the air of the cabinet. The upward trend of the peripheral temperature of the right thigh, which was apparently induced by placing the animal in the heated cabinet, was not affected by injection of the inflammatory agent.

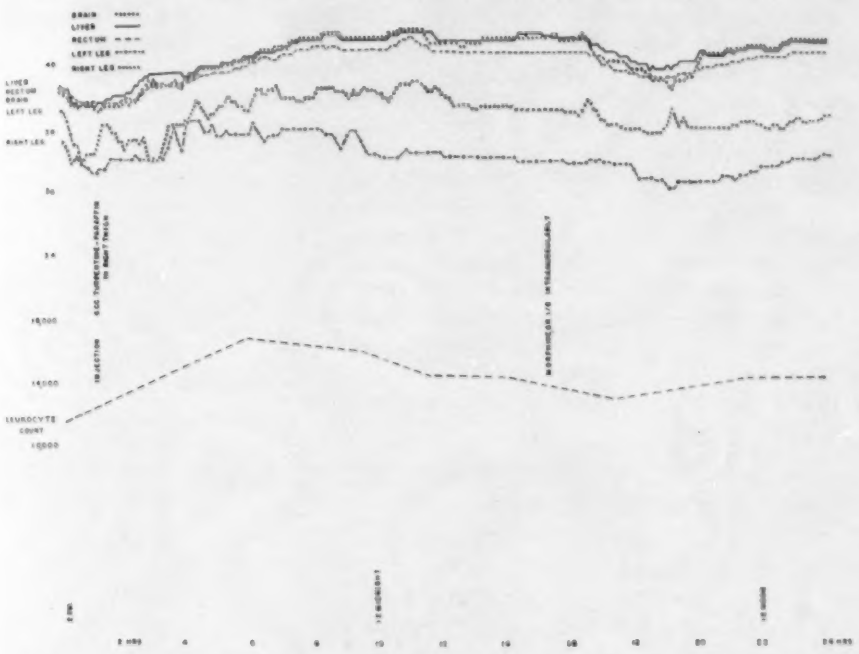

Chart 1.—Data on experiment 9. Six cubic centimeters of amytal was administered.

INFECTION

In experiments 11 to 15 observations were made on the deep temperature and on the leukocytic response after production of a localized acute infection. All experiments were of twenty-four hours' duration; readings were made every ten minutes. Thermocouples were placed in the brain, the liver, the rectum and the muscles of the thighs. The room temperature was 24 to 28 C. The humidity was 20 to 40 volumes per cent.

EXPERIMENT 11.—A dog weighing 12.5 Kg. was given 0.8 Gm. of amytal intraperitoneally. The temperatures of the deep organs were not unusual in their

behavior in comparison with the readings obtained in earlier experiments. One-half hour after the thermocouples had been placed, 3 cc. of a broth suspension (containing 2,000,000,000 organisms to a cubic centimeter) of Staph. aureus was injected into the muscles of the right thigh, approximately at the point to which the thermocouple had been inserted. There was an immediate rise in the regional temperature from 31 to 35 C. This was followed by a drop, and the higher level was not approached again until three hours later. The maximal elevation of the white blood cell count occurred seventeen hours after injection of the organisms.

EXPERIMENT 12.—A dog weighing 11.5 Kg. was given 0.8 Gm. of amytal intraperitoneally. In this experiment the technic was exactly the same as in the

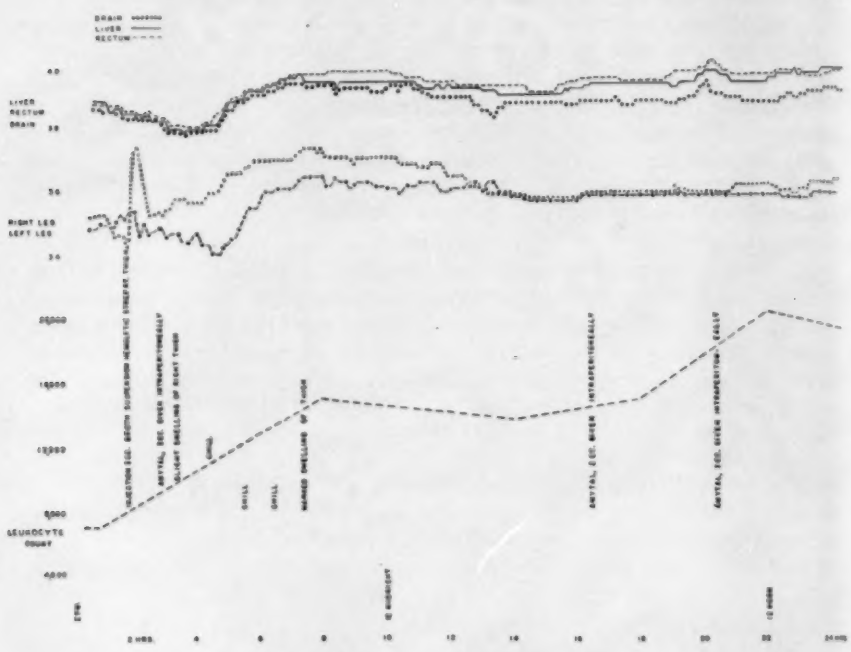

Chart 2.—Data on experiment 15.

preceding one (experiment 11), except that 6 cc. of a broth suspension (about 2,000,000,000 organisms per cubic centimeter) of Staph. aureus was injected into the muscles of the right thigh. The temperature curves were similar to those of the preceding experiment. The muscular temperature of the infected leg was elevated above that of the normal leg for nine hours, then fell to a lower level. The systemic temperatures as measured in the brain, liver and rectum showed a persistent rise. The leukocyte count reached its maximum later than it did in the experiments dealing with acute inflammation. It rose from 9,000 to 26,000 per cubic millimeter in ten hours.

EXPERIMENT 13.—A dog weighing 13 Kg. was given 0.8 Gm. of amytal intraperitoneally. In this experiment 6 cc. of a suspension of Staph. aureus in whole blood (about 2,000,000,000 organisms to the cubic centimeter) was injected into

the right thigh. In comparison with the 2 earlier experiments (11 and 12) it was observed that the deep temperatures were higher, reaching 41.4 C. Similarly, the regional temperature in the infected leg reached 38.8 C., a level which was 1.5 degrees higher than the highest peripheral temperature observed in experiments 11 and 12. The leukocyte count rose slowly from 11,000 per cubic millimeter to a peak of 21,800, which was reached sixteen hours after the injection.

EXPERIMENT 14.—A dog weighing 14 Kg. was given 0.9 Gm. of amytal intraperitoneally. Six cubic centimeters of a saline suspension of Staph. aureus (about 2,000,000,000 organisms to the cubic centimeter) was injected into the muscular tissues about the point of the thermocouple inserted into the right thigh. The peripheral temperature (muscle of the right thigh) reached a height greater than had been previously observed, 39.4 C., keeping pace with the elevation in deep temperatures (brain, liver, rectum) to 41 C. The leukocyte count rose from 7,000 to 25,000 per cubic millimeter after twenty-one and one-half hours.

EXPERIMENT 15.—A dog weighing 15.5 Kg. was given 1 Gm. of amytal intraperitoneally. Three cubic centimeters of a broth suspension of beta hemolytic streptococcus (about 2,000,000,000 organisms to the cubic centimeter) was injected into the muscles of the right thigh of the animal about the point of the thermocouple. There was a distinct rise in the deep temperatures after the injection. This was irregularly maintained throughout the twenty-four hour period. The initial rise of the temperature in the muscles of the infected thigh after the injection was followed by an elevation which persisted for twelve hours. The temperature of the leg then dropped to approximately that of the outer extremity. The leukocyte count slowly rose from the starting point of 7,000 per cubic millimeter to a peak of 20,400 at the twenty-second hour. The drop in peripheral temperature at the site of infection was concomitant with the occurrence of signs of edema at that area.

SUMMARY AND COMMENT

Detailed report is made of observations on deep tissue temperatures as affected by experimentally induced inflammation and infection in a series of 15 experiments. In 9 of these, observations were made over a twenty-four hour period. The first 5 experiments were planned to give information as to the normal variations of the temperatures of these parts (liver, brain, rectum, muscles) after several anesthetic agents were administered. Evidence is presented that amytal introduced into the peritoneal cavity gives a very satisfactory control of the animals for this type of experimental study. The deep temperatures were more constant after administration of amytal than after administration of morphine, avertin with amylene hydrate or procaine hydrochloride. Amytal was, therefore, selected as the anesthetic of choice for the experiments. It was found that variations of 0.5 degree centigrade in the temperature of the liver, brain or rectum were common and of no significance, the highest temperature or the lowest temperature being exhibited by any one of the organs at different times. It was also found that a variation of 1 degree centigrade in temperature of the room was without effect on the temperatures of the deep organs or tissues.

From a study of the experiments (6 to 10) dealing with aseptic inflammation the following inferences may be drawn:

1. Injection of an inflammatory agent into the muscular tissues of the periphery is accompanied by an immediate rise in local temperature.

2. Production of an acute peripheral inflammation is followed within a few hours by an increase in the deep temperatures as measured in the liver, brain and rectum.

3. The peripheral temperature at the site of the localized inflammation may decline as swelling develops at the site, although the deep temperatures continue to rise or remain elevated.

4. The leukocyte count shows a steady increase during the first ten to twenty hours after the production of an acute localized peripheral inflammation, its maximum not being reached until a varying number of hours after the peak of the peripheral temperature.

5. In the first twenty-four hours after the initiation of an acute localized peripheral inflammation the temperature of the infected area does not exceed that of the deep organs (liver, brain, rectum).

It is further indicated by experiment 10 that a peripheral inflammation does not cause an increase in local temperature in an extremity previously subjected to increase in temperature by inclusion in a heated cabinet. In the experiment referred to, the temperature of the tissues in which inflammation was to be induced had shown a significant elevation after the posterior extremities of the animal were placed in a heated cabinet. In none of the experiments recorded herein did the local temperature at the site of acute inflammation at any time exceed that of the deep organs. This observation leads to the impression that elevation of the temperature of peripheral tissues in association with acute inflammation is due chiefly to the induced hyperemia rather than to specific biochemical or metabolic processes at work in the area of cellular change. It is recognized, however, that this evidence is hardly sufficient to rule out the factor of local increase in metabolism of tissue as a cause of heat production.

The frequency of readings in the experiments reported affords information as to the order and sequence of the rise in temperature of the organs and tissues in which observations were made. The variations observed in the rise in temperature of the muscles of the leg in the different experiments, these having been carried out with the same technic in all cases, are not easily explained, nor are the variations in the degree of leukocytosis and in the time at which there was maximal leukocytosis. Attention is called to the fact that the value of the observations reported here lies in the comparative study of the relation of the abnormal temperatures of the disturbed peripheral tissues to

those of similar tissues and to the temperatures of the deep intracranial and intra-abdominal organs, both in the degree of heat production and in the rate of its development. It is pointed out further by these observations that the fluctuations in temperature of an acutely inflamed peripheral zone do not parallel the rise in general temperature of the body as measured in the internal organs (brain, liver, rectum). That the elevated temperature in these organs remains persistently at a higher level than those of the inflamed region suggests that since, in the process of circulation, the blood passes through the intra-abdominal organs before being transferred to the periphery, the increased warmth of the inflamed area is due not to local production of heat but to transference of heat to the area by the increased rate of flow of blood (hyperemia). This impression was obtained in working with inflammatory processes (experiments 6 to 10) and also with infection (experiments 11 to 15).

In brief summation of the experiments dealing with infection (experiments 11 to 15) it may be concluded that:

1. Injection of an infectious agent into the muscular tissues of the periphery is accompanied by an immediate rise in local temperature, this rise being, in general, higher than that observed in the experiments dealing with sterile inflammation.

2. Production of an acute peripheral infection is followed within a few hours by a rise in the temperatures of the deep organs, just as observed in the experiments dealing with inflammation.

3. In the twenty-four hour period immediately following initiation of the infection the temperature in the infected zone rises and then falls when suspensions of staphylococci are injected. The peripheral temperature is maintained at a higher level when suspensions of streptococci are injected. The deep temperatures continued to rise or remain elevated throughout the period of observation just as in the experiments in sterile inflammation.

4. Leukocytosis is not maximal as early after the production of an acute infection as after the start of an acute inflammation.

5. After the initiation of an acute localized peripheral infection, the temperature of the infected area does not exceed that of the deep organs.

6. The regional and general responses of temperature after an acute infection has been produced are not appreciably different when the organisms are suspended in physiologic solution of sodium chloride, broth or whole blood.

A comparison of these findings with those of other investigators may be made. The work of Maximov,[3] who demonstrated by a series of

3. Maximov, cited by Segale, M.: Temperature of Acutely Inflamed Tissues, J. Exper. Med. **29**:235, 1919.

accurate temperature determinations carried out with thermoelectric batteries that in no part of the inflammatory process is the temperature higher than that of the heart's blood or the blood of the larger vessels is confirmed by these observations. Similarly, the contention of Jacobson,[4] Bernard,[5] Schneider[6] and Ruppert,[7] namely, that if the inflamed area has a higher temperature than that of the corresponding area, it cannot be asserted that its temperature is above that of the central blood, is confirmed. Marchand,[8] in a summary of the results of a study of this subject, concluded that the increased flow of blood is the responsible factor in heat production, rather than a disturbing element. It was suggested by Bernard that the flow of blood to a part might be considered the result of local calorification. After exhaustive thermometry studies, in which it was demonstrated that the temperature of the blood in the hepatic vein is consistently warmer than that in the portal vein, he (Bernard) came to the conclusion that the blood actually is warmed by certain organs but that there is no one organ which generates heat; it is a function of all tissues which are subject to nutrition. Cavazzani[9] recorded an increase in temperature of the hepatic parenchyma after blocking the circulation in the hepatic artery and portal vein. Segale,[10] supporting Cavazzani's work, reported 6 animal experiments in which the temperature in the inflamed area was observed to rise after the production of ischemia in the part or after the death of the animal. Krehl and Kratzsch[11] found that in animals with fever the liver is as warm as in normal animals or warmer. Schade, Haagen and Schmidt,[12] in disputing Marchand's belief that the increased local heat in inflamed tissue is due to the afflux of blood to the affected part, demonstrated that the temperature of the inflamed area rose 0.1 degree

4. Jacobson, H.: Ueber normale und pathologische Temperaturen, Virchows Arch. f. path. Anat. **51**:275, 1870.

5. Bernard, C.: Leçons sur la chaleur animale, sur les effets de la chaleur et sur la fièvre, Paris, J. B. Baillière, 1876.

6. Schneider, O.: Einige Beobachtungen über den Stoffwechsel bei künstlicher Plethora und Anämie, Marburg, C. L. Pfeil, 1861.

7. Ruppert, M., cited by Segale.[10]

8. Marchand, F.: Die thermischen Krankheitsursachen, in Krehl, L., and Marchand, F.: Handbuch der allgemeinen Pathologie, Leipzig, S. Hirzel, 1908, vol. 1, chap. 2.

9. Cavazzani, E.: Sul differenziamento degli organi della sensibilita termica de quelli del senso di pressione, Riforma med. **8** (pt. 1):797-801, 1892.

10. Segale, M.: Temperature of Acutely Inflamed Peripheral Tissue, J. Exper. Med. **29**:235, 1919.

11. Krehl, L., and Kratzsch: Untersuchungen über die Orte der erhöhten Wärmeproduktion in Fieber, Arch. f. exper. Path. **41**:185, 1898.

12. Schade, H.; Haagen, W., and Schmidt, K.: Thermoelektrische Messung der Wärmeverhältnisse an Ort der Entzündung, Zentralbl. f. d. ges. exper. Med. **83**:343. 1936.

above the rectal temperature. In the experiments of Schade, Haagen and Schmidt, localized inflammation was produced by the injection of turpentine-paraffin solution twenty-four hours before the observations were made. In our own experiments the temperature of the inflamed area was not at any time found to be higher than that of the liver, brain and rectum.

In keeping with van't Hoff's law, Shorr,[13] working with tissues in vitro (Warburg technic), has observed a tremendous increase in tissue metabolism in the presence of infection. Similarly, Gessler [14] concluded after extended experimental studies that the effect of external heat is a great increase in metabolism of tissue with subsequent hyperemia. In our experiments the degree of elevation of peripheral temperature has been greater in the experimental infections than in the inflammations. This is in keeping with Shorr's observation. There is, however, no conclusive evidence that increased metabolism is responsible for increased production of heat.

Returning again to the role of the circulating blood and its possible effect on the area of the increased temperature as a cooling or heating phenomenon, attention is called to the classic experiments of Ludwig and Spiess,[15] confirmed by Burton-Opitz,[16] in which it was demonstrated that in cases of parotitis there are marked local heating and an elevation of temperature above that of the regional arterial blood, the venous blood being warmer than the arterial blood. Also, as has been mentioned, Schade made observations showing that the temperature at the site of the infection rose above that of the rectum. On the other hand, one of us (Conway [17]) has reported on regional temperatures in carbuncles in man. In only 2 of 20 cases was the temperature in the acutely inflamed zone even a fraction of a degree above the rectal temperature taken at the same time. Also, the regional temperatures in the infected areas were consistently higher in that portion of the carbuncle in which hyperemia was maximal.

The reports in the literature relating to temperatures in infected areas are few. To our knowledge, diurnal temperature readings following experimental inflammation and infection as recorded herein have not previously been made. All of the information made available

13. Shorr, E.: Personal communication to the authors.

14. Gessler, H.: Ueber Entzündung, Arch. f. exper. Path. u. Pharmakol. **163**: 477, 1931.

15. Ludwig, C., and Spiess, A., cited by Segale.[10]

16. Burton-Opitz, R.: Ueber die Temperatur des Chorda- und des Sympathikusspeichels, Arch. f. d. ges. Physiol. **97**:309, 1903.

17. Conway, H.: Subcutaneous Temperatures in Localized Infections, Proc. Soc. Exper. Biol. & Med. **34**:353, 1936.

through these experiments has supported, though not conclusively, the belief that the increase in local heat at the site of an acute inflammation or infection is occasioned by the warmth brought to the site by the increased afflux of blood. While the temperature of the circulating blood probably is dependent on cellular biochemical activity and metabolism in the tissues, there is nothing in the results of these experiments to indicate that these forces are augmented as producers of heat at the site of an acute localized inflammation or infection.

Dr. M. E. Pickworth, of San Jose, Calif., assisted in the management of the experiments.

STUDIES IN THE ETIOLOGY OF ACUTE APPENDICITIS

AN INQUIRY INTO THE FACTORS INVOLVED IN THE DEVELOPMENT OF ACUTE APPENDICITIS FOLLOWING EXPERIMENTAL OBSTRUCTION OF THE APPENDICAL LUMEN OF THE RABBIT

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MINNEAPOLIS

PURPOSE OF THIS INVESTIGATION

The secretion of fluid by the appendix of man, the chimpanzee and the rabbit and the development of appendicitis consequent to obstruction of the appendical lumen in these species have been reported.[1] Twenty-four other species of animals have failed to show either secretion of fluid or development of appendicitis following obstruction by ligation.[2]

The rabbit has proved so useful an animal in which to study the effects of appendical obstruction that it is believed worth while to outline the results of the experiments which have been done on this species. Further, it is possible in the rabbit, in which the functional behavior of the cecal appendage in many respects is not unlike that of the vermiform process of man, to make controlled observations which cannot

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1. (*a*) Wangensteen, O. H.; Buirge, R. E.; Dennis, C., and Ritchie, W. P.: Studies in the Etiology of Acute Appendicitis: The Significance of the Structure and Function of the Vermiform Appendix in the Genesis of Appendicitis, Ann. Surg. **106**:910, 1937. (*b*) Wangensteen, O. H., and Dennis, C.: The Production of Experimental Acute Appendicitis (with Rupture) in Higher Apes by Luminal Obstruction, Surg., Gynec. & Obst. **70**:799, 1940. (*c*) Wangensteen, O. H., and Dennis, C.: Experimental Proof of the Obstructive Origin of Appendicitis in Man, Ann. Surg. **110**:629, 1939.

2. Dennis, C.; Buirge, R. E., and Wangensteen, O. H.: An Inquiry into the Functional Capacity of the Cecal Appendage in Representative Birds and Mammals, Surgery **7**:372, 1940.

be done on man, and such observations also are of the greatest value in promoting understanding of the effects of luminal obstruction of the appendix of man. It is the special object of this paper to indicate the extent of the secretory capacity of the cecal appendage of the rabbit, the effects of obstruction and the factors which alter secretory capacity and the effects of obstruction.

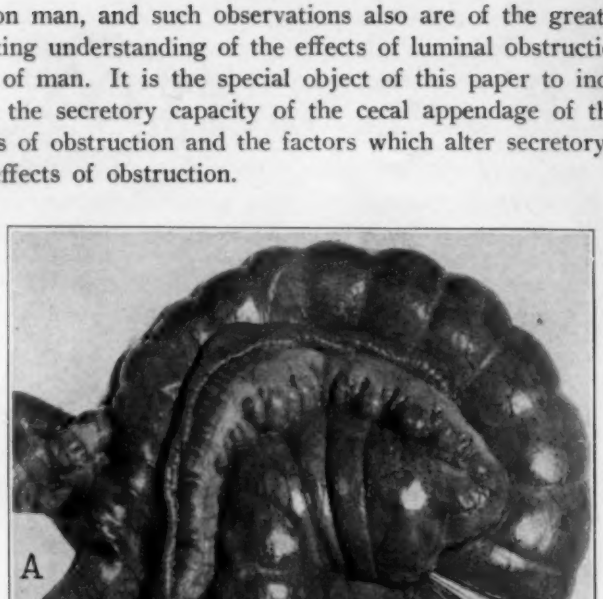

Fig. 1.—Photograph of the normal cecum and adjacent structures of the rabbit. The cecal pouch is very thin walled, coiled, about 30 cm. long and in its widest diameter roughly 6 cm.; at the distal end it is capped by the cecal appendage (*A*), which is sharply demarcated from the gray-green cecum by its reddish yellow color and the lymphoid follicles which show through the thin muscularis and serosa. The appendage has an average length of 6 to 9 cm. The blood supply comes from the superior mesenteric vessels; a part passes down near the appendage in the mesentery, and the rest comes across the mesentery in a dozen vessels from the ileum (*I*). *C*, colon. A forceps is placed on the ileocecal valve.

MATERIALS

Two hundred and thirty-five rabbits were used in the experiments reported here. The cecal pouch of the rabbit is very thin walled, about 30 cm. long and in its widest diameter roughly 6 cm. wide; at the distal end it is capped by the cecal appendage, or appendix, which is sharply demarcated from the gray-green cecum

by its reddish yellow color and the lymphoid follicles which show through the thin muscularis and serosa. The appendage (fig. 1) has an average length of 6 to 9 cm.; its diameter varies from 8 to 15 mm.; it is about as thick walled as the human appendix (averaging 1.5 mm. in 13 cases), but the muscularis is much less prominent (averaging about 20 microns in 13 cases), the remainder of the wall being composed of abundant lymphoid tissue and mucosa. The microscopic appearance is shown in figure 2; there are large lymphoid villi covered with epithelium, and between these and extending over them are masses of glandular and epithelial tissue on narrow pedicles. The blood supply comes from the superior mesenteric vessels; a part passes down near the cecal appendage in the mesentery, and the rest comes across the mesentery in a dozen vessels from the ileum.

The cecal appendage of the rabbit therefore differs from the vermiform process of man in having a larger lumen without possibility of spontaneous obstruction, a thinner muscularis and a different configuration of the mucosa and lymphoid tissue. Certain differences in cellular reaction to inflammation have been discussed in a report on cytologic responses.[3]

PROCEDURES

Anesthesia was routinely induced by pentobarbital sodium given intravenously, except in a few short procedures in which ether was used. Aseptic surgical procedure was, of course, used throughout. A doubled suture of commercial no. 30 linen was placed loosely around the base of the appendage 1 to 2 cm. distal to its junction with the cecum, being passed between the organ and the longitudinal vessels in order to spare the blood supply. Two fine silk purse strings were laid, one 5 mm. from the tip of the appendage and the second 5 mm. behind the first. The tip was punctured for insertion of a glass cannula, which was fastened with the distal purse string, the second being used for inversion of the intervening 0.5 cm. of appendage over the cannula, a procedure found necessary to prevent leakage. The contents of the appendage were washed into the cecum with 5 to 25 cc. of fluid, usually 0.9 per cent solution of sodium chloride, and the base was obstructed by ligation of the previously placed ties. The wound was closed, the cannula being allowed to emerge at one end. In prolonged experiments anesthesia was usually maintained by subcutaneous injection of pentobarbital sodium or amytal sodium; in many cases the anesthetic was continuously administered, together with the daily fluid and sodium chloride requirement, by an electrically driven syringe. In certain cases simple ligation was performed. Variations from these procedures will be detailed with the results.

MICROSCOPIC CLASSIFICATION OF LESIONS PRODUCED

The microscopic changes associated with experimental obstruction of the rabbit cecal appendage have been described elsewhere.[3]

RESULTS

I. *Proof of the Secretory Capacity of the Rabbit Cecal Appendage.*—When the obstructed, incannulated rabbit appendages were connected to recording manometers, there was uniformly present a rapid rise in intraluminal pressure. This rise was, of course, more rapid with the

3. Buirge, R. E.; Dennis, C.; Varco, R. L., and Wangensteen, O. H.: The Histologic Picture of Experimental Appendical Obstruction (Rabbit, Ape and Man), Arch. Path., to be published.

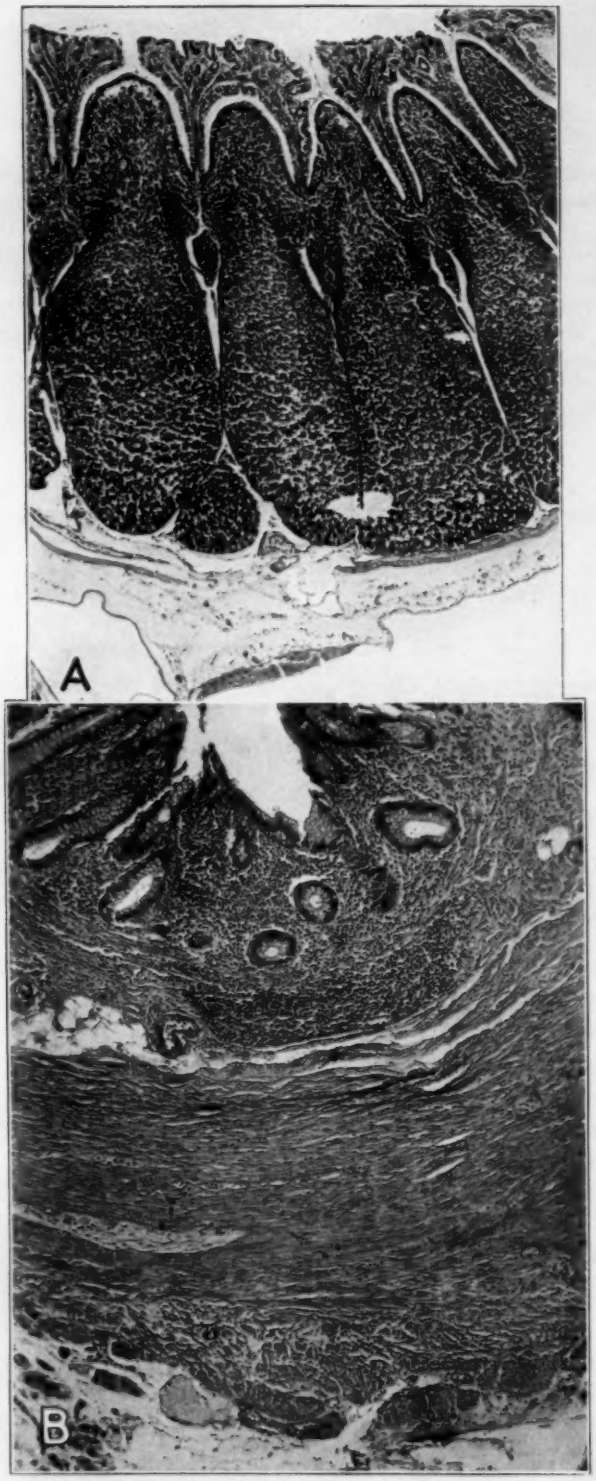

Fig. 2.—*A*, photomicrograph of the normal cecal appendage of a rabbit (× 50). The appendage is about as thick walled as the human appendix (1.5 mm.), but the muscularis is much less prominent (20 microns), the remainder of the wall being composed of abundant lymphoid tissue and mucosa. There are large lymphoid villi covered with epithelium and, between these and extending over them, masses of glandular and epithelial tissue on narrow pedicles. *B*, photomicrograph of a normal human appendix (× 60). The muscularis is much more prominent than in the rabbit's appendage.

use of a small volume manometer (requiring ejection of 1 cc. of fluid from the appendage to elevate the reading 100 cm. of water) than with the use of a large volume instrument (requiring ejection of 20 cc. of fluid by the appendage for the same rise in pressure [fig. 3]).

When apparatus was prepared to permit maintenance of a constant pressure head against any secretory activity which the appendage might exhibit, the fluid was poured out in each of 26 experiments performed. The rate of ejection of fluid by the appendage varied from 20 to 80 cc. daily, varying primarily with the passage of time (fig. 4). In 19 cases of ligation and incannulation, rubber condoms were attached to the

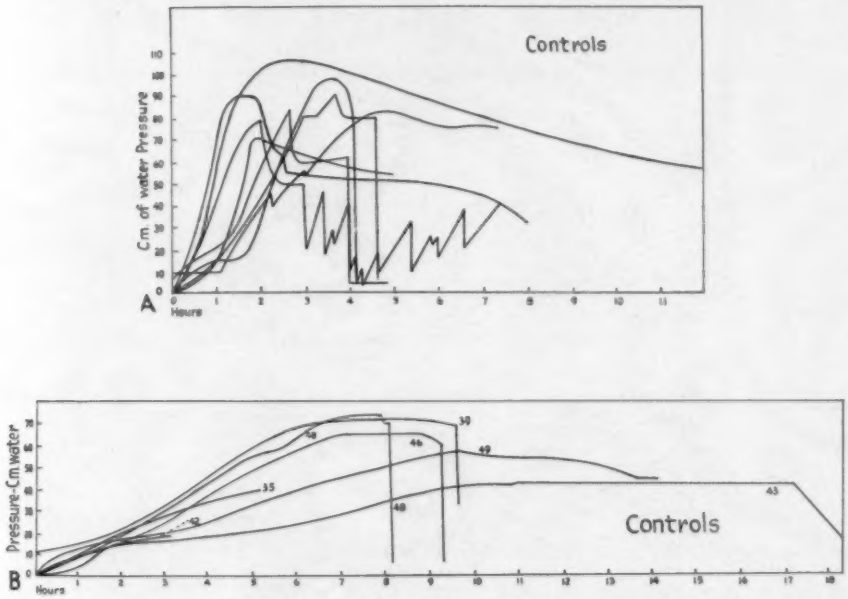

Fig. 3.—*A*, rate of rise in pressure in the obstructed, incannulated rabbit cecal appendage. (Apparatus: 1 cc. = 100 cm. of water.) *B*, rate of rise in pressure in the obstructed, incannulated rabbit cecal appendage. (Apparatus: 20 cc. = 100 cm. of water.)

cannulas and dropped into the abdomens, the rabbits being allowed to recover. Fluid uniformly accumulated in the condoms, occasionally in sufficient quantity to cause evident abdominal distention.

II. *Effects of Increased Intraluminal Tension.*—Pathologic changes in the wall of the rabbit appendage occur as a result of the rise in intraluminal pressure following ligation near the base. In all cases of complete obstruction in which the process was not artificially interrupted either seepage or gross rupture occurred. As has been described for the human appendix,[4] seepage often occurs in sufficient quantity

4. Dennis, C., and Wangensteen, O. H.: Unpublished data.

to permit the escape of fluid rapidly enough for a fall in intraluminal pressure to occur. Examples of both seepage (gradual fall in pressure) and rupture (abrupt fall in pressure) are shown in figure 3. Occasionally peritoneal sealing occurred sufficiently fast to permit rise of pressure after rupture, and in rare instances this happened many times in the same preparation (fig. 3 *A*).

The amount of stretching of the appendical wall was judged by change in luminal volume, which was determined at either 10 or 20 cm.

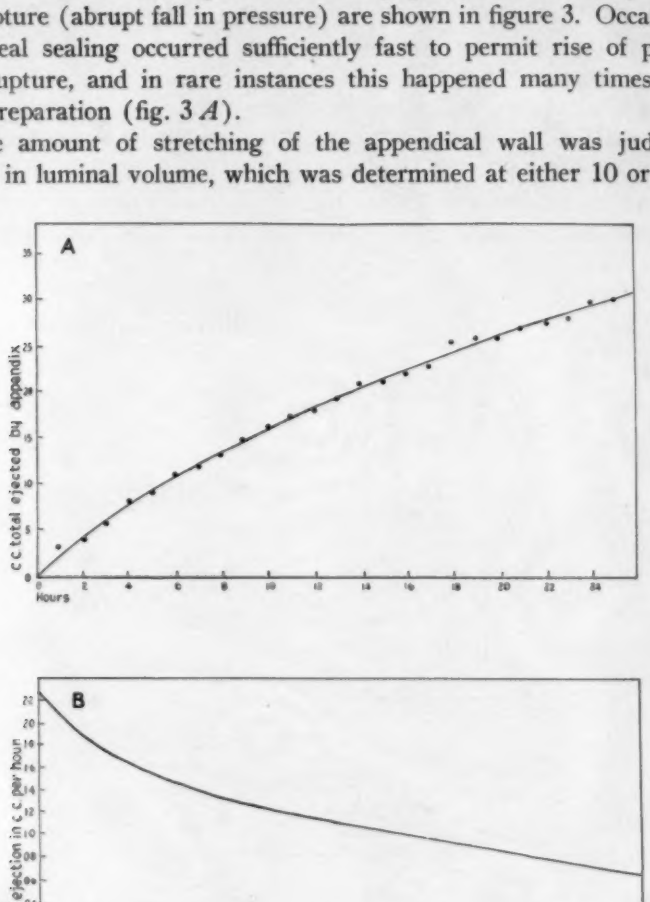

Fig. 4.—Changes in rate of ejection of fluid against 5 cm. of water pressure by an incannulated, obstructed rabbit cecal appendage. *A*, absolute amount ejected; *B*, rate of ejection in cubic centimeters per hour.

of water pressure by attaching the cannula in the appendage to a T tube, one arm of which led to a volume-calibrated manometer and the other to a calibrated syringe. Marked stretching of the wall of the appendage occurred as the pressure rose after obstruction, the amount of increase in luminal volume depending more on the duration than on the amount of the increase in pressure (table 1).

Histologic changes characteristic of acute appendicitis were regularly encountered when sufficient time had been allowed to elapse after ligation. That these changes were not the result of faulty technic is demonstrated by a series in which the appendage was ligated 2 cm. distal to the true base and sections were taken at the conclusion of the experiment from the segment proximal to the tie as well as distally (table 2). In 13 experiments significant acute appendicitis was encountered in all but 1 specimen distal to the tie (the one exception being in a four-hour experiment, near the lower time limit for histologic changes), while 12 of the 13 animals either were normal or presented the inconsequential

TABLE 1.—*Luminal Volume Changes During Recordings of Rabbit Cecal Appendages* *

Rabbit	Duration of Experiment, Hours	Maximum Pressure, Cm. of Water	Initial Volume, Cc.	Final Volume, Cc.
116	9	35 plus	6.2	25
125	8	82	0.9	4
126	4	70	3.8	6
127	8	41 plus	7.0	27
136	9	85	2.5	4.2
137	29	46	1.6	8.1
142	6	95	0.8	3
145	20	40	1.1	25
146	26	23 (constant)	Not done	9
149	46	20 (constant)	Not done	25 (approx.)
150	29	20 (constant)	Not done	16
152	21	6 (constant)	2.6	6.4
157	24	20 (constant)	Not done	17
160	70	20 (constant)	Not done	20
	—	—	—	—
Mean			3.0	13.8

The small initial volumes recorded in this table are due largely to the rigidity implied by the presence of the cannula and inversion over it, for when 4 normal appendages were removed and incannulated at the base without inversion, the volumes at 10 cm. of water pressure averaged 5.3 cc.

*Determined at a pressure of 10 cm. of water.

picture of serosal appendicitis [3] proximally. The specimen which showed acute inflammation proximally showed gangrene distally and had been allowed to wait eight days after ligation.

In order to determine the effect of prolonged maintenance of pressure in the living appendage on the pressure required to rupture the organ, comparisons were made between the rupturing pressures with the "rapidly rising small volume apparatus," with the "slowly rising large volume apparatus" (both of which have been described) and finally by acutely distending normal appendages. In this manner it was found that rapid deterioration of the wall occurred under the influence of increased intraluminal pressure, so that the bursting pressure was cut to one half in less than twelve hours (table 3). This conclusion is

in agreement with that of Sperling and Wangensteen [5] as to the dog's intestine in simple obstruction.

III. *Proof that Pathologic Changes Are Not Due to Ligation Proper Rather than to Increased Intraluminal Pressure.*—That the

TABLE 2.—*Control Data on Rabbit Appendicitis*

Rabbit	Duration of Obstruction	Microscopic Diagnosis of Condition Distal to Ligature*	Microscopic Diagnosis of Condition Proximal to Ligature*
191	4 hours	Serosal appendicitis, grade 1	Serosal appendicitis, grade 1
192	4 hours	Mucosal appendicitis, group A, grade 2	Normal
176	4 hours	Diffuse appendicitis, grade 1	Normal
183	4½ hours	Mucosal appendicitis, group A, grade 1	Serosal appendicitis, grade 1
178	9¼ hours	Mucosal appendicitis, group A, grade 3	Serosal appendicitis, grade 1
175	10 hours	Diffuse appendicitis, grade 2 (gangrenous)	Serosal appendicitis, grade 2
197	10¾ hours	Mucosal appendicitis, group B, grade 4	Normal
177	20 hours	Diffuse appendicitis, grade 1	Serosal appendicitis, grade 1
184	22 hours	Mucosal appendicitis, group B, grade 4	Serosal appendicitis, grade 2
187	24 hours	Mucosal appendicitis, group B, grade 4 (gangrenous)	Normal
190	2 days	Diffuse appendicitis, grade 2	Serosal appendicitis, grade 2
194	5 days	Healing appendicitis, granulocytes	Serosal appendicitis, grade 1
195	8 days	Healing appendicitis; granulocytes (gangrenous)	Mucosal appendicitis, group A, grade 1, healing

* The ligature was placed 2 cm. distal to the true base.

TABLE 3.—*Effect of Prolonged Maintenance of Elevated Intraluminal Pressure on Bursting Pressures of Rabbit Cecal Appendages*

Normal Appendage, Acutely Distended:	With Small Volume Apparatus		With Large Volume Apparatus	
Pressure, Cm. of Water	Time, Hours	Pressure, Cm. of Water	Time, Hours	Pressure, Cm. of Water
150	4	85	8¼	72
140	4.1	90	9½	71
120	2	79	9½	66
140	2	86	13¾	57
			17¼	43
Mean 137½	3.03	85	11½	61.3

pathologic changes observed were not due to ligation of the appendical base rather than to the secondary rise in pressure is evidenced by 2 experiments in which the base was ligated and incannulated in the

5. Sperling, L., and Wangensteen, O. H.: Influence of Obstruction of the Bowel on Its Strength (Bursting Strength), Proc. Soc. Exper. Biol. & Med. **32**: 1183, 1935.

usual fashion but in which the pressure was not allowed to rise above 5 cm. in the one case and 6 cm. in the other. After sixty-seven and twenty-one hours, respectively, the specimens showed inconsequential [3]

TABLE 4.—*Fate of Rabbit's Cecal Appendage Subjected to Simple Ligation Obstruction at the Base*

Duration	Rabbit	Abdominal Mass Palpable	Distended	Serosal Tear	Rupture	Gangrene	Adhesions	Peritonitis (General: G Local: L)	Serosal Appendicitis	Mucosal Appendicitis, Group A	Mucosal Appendicitis Group B	Diffuse Appendicitis	Healing Appendicitis
1 hour	180	0	0	0	0	0	0	0	..	..	..	..	..
3 hours	182	0	0	0	+?	0	+	L	..	..	..	..	..
4 hours	191	0	++	0	0	0	0	0	1	..	..	..	..
4 hours	176 Wa WI	0	+	0	0	0	0	0	..	..	..	1	..
5 hours	BD1	0	++	0	0	0	0	0	..	..	..	1	..
5 hours	BD2	0	+++	0	0	0	0	0	..	..	3	..	..
6 hours	BD19	0	+	0	0	0	0	0	..	2	..	..	..
6 hours	BD20	0	+	+	0	0	0	0	..	..	3	..	..
7½ hours	BD10	0	0	+	+?	+	0	L	..	..	3	..	..
7½ hours	BD11	0	+	0	0	0	0	0	..	2	..	..	..
8 hours	188	+	0	—	+	0	+	G	..	..	..	..	..
9 hours	178 WI	—	0	—	+	+	+	L	..	3	..	..	..
10½ hours	175 Wa WI	—	++	0	0	+	+	0	..	..	..	2	..
11½ hours	165 WI	—	0	—	+	+	+	G	..	..	..	1	..
19 hours	177 WI	—	0	—	+	0	+	0	..	..	..	1	..
24 hours	187	+	?	—	+	0	++	0	..	..	4	..	..
30 hours D	55	?	+	—	+	+	+	G	..	..	4	..	..
48 hours	190	+	?	—	+	0	++	G	..	..	..	2	..
4 days D	180	0	0	—	+	+	++	0	..	..	..	2	..
9 days D	195	?	0	—	+	0	+	G	..	..	..	..	+†
9 days	44 Wa	+	0	—	+	+	++	G	..	..	..	..	+†
9 days	45 Wa	?	+	—	+	0	+	G	..	..	..	..	..
3 months D	193	+	*	..	..	+++	++++	G++	..	..	..	..	..

* This appendix had become necrotic beyond recognition and was lost in a mass of adhesions stronger than the remaining bowel. Numerous small pockets of pus and caseous material were to be found on cutting into this mass.

The figures below the group classifications of the type of appendicitis indicate the grade.

"Wa" indicates that the lumen of the appendix was washed through a cecostomy prior to obstruction.

"WI" indicates that a window was inserted into the abdominal wall for observation of the course of events. "D" indicates that the animal died of the disease; in all other cases the appendixes were obtained surgically or by killing the rabbit.

† Healing appendicitis with polymorphonuclears.

serosal appendicitis (type I) in the one case and no inflammation in the other (although there was edema of the mucosal pedicles).

IV. *Effect of Simple Ligation of the Rabbit Cecal Appendage.*—In order to learn the course of events consequent to simple obstruction of the rabbit cecal appendage, ligation near the base was performed in a series of 22 animals, and reexamination was made at intervals thereafter varying from one hour to three months (table 4). Masses due to

dense and extensive adhesions were palpable through the intact abdominal wall in a large number of experiments in which eight hours or more had been allowed to pass after ligation; in this group perforation and peritonitis were the rule. With the lapse of time the appendage fills tensely, and areas on the surface become blanched and ischemic, occasionally hemorrhagic and finally often gangrenous; at about eight hours rupture usually occurs, releasing tension and culminating in local and then in general peritonitis and extensive formation of adhesions. The microscopic picture is at first only that of serositis but is later more involved, with granulocytes diffusely spread (diffuse appendicitis) or chiefly collected in an infectious process in the mucosa (mucosal appendicitis, group A) or with primarily an infarction of much of the mucosa and only secondary inflammation (mucosal appendicitis, group B). These changes were in general increasingly severe with the passage of time up to forty-eight hours, but at nine days healing processes were well established. Unless killed early, the animals almost invariably died of complications of the disease.

In order to check the relation of changes in pressure to the rate of stretch of the appendical wall, 4 rabbits were subjected to simple ligation, and glass windows were placed in the abdominal wounds, the air in the abdomens being displaced by isotonic sodium chloride solution. The changes in diameter of the appendages are illustrated in figure 5. The dotted curve is a theoretic one, disregarding the thickness of the walls and based on the suppositions that the increase in luminal volume is constant in rate and that an hour was required to fill the appendage initially. The closeness of the curves representing experiments in which rupture did not occur early to the theoretic curve justifies the supposition that the rate of increase in volume is roughly constant until rupture.

During the experiments with the abdominal window it was also possible to observe changes in the appendical wall with advancing distention. The appendix regularly was tense within an hour or two, and shortly the whole organ became somewhat blanched, occasionally with slight movements and obliteration of first the smaller and later the larger vessels. Peristalsis in the ileum became decreased, irregular or (often) reversed in direction at two to three hours, and these changes persisted, though activity in general diminished markedly. At three to four hours some of the lymph follicles seen through the appendical wall commenced to show petechial hemorrhages and others to become acutely blanched, one or two at first and then more, till at seven or eight hours nearly all were blanched, many with petechiae about them. At six to eight hours larger areas, 5 to 20 mm. across, became obviously devoid of blood supply, and in other areas larger hemorrhages appeared. Finally the ischemic areas broke down and bacame necrotic, and rupture

ensued. It seems likely, therefore, that this was a process of ischemic necrosis.

V. *Proof of the Absorptive Function of the Cecum.*—The question arose whether the cecum as well as the appendage pours fluid into the lumen. This was settled with a single animal by ligation of the cecum 5 cm. distal to the ileocecal valve and incannulation just distal to the tie, a blind segment being made of the secum and appendix together.

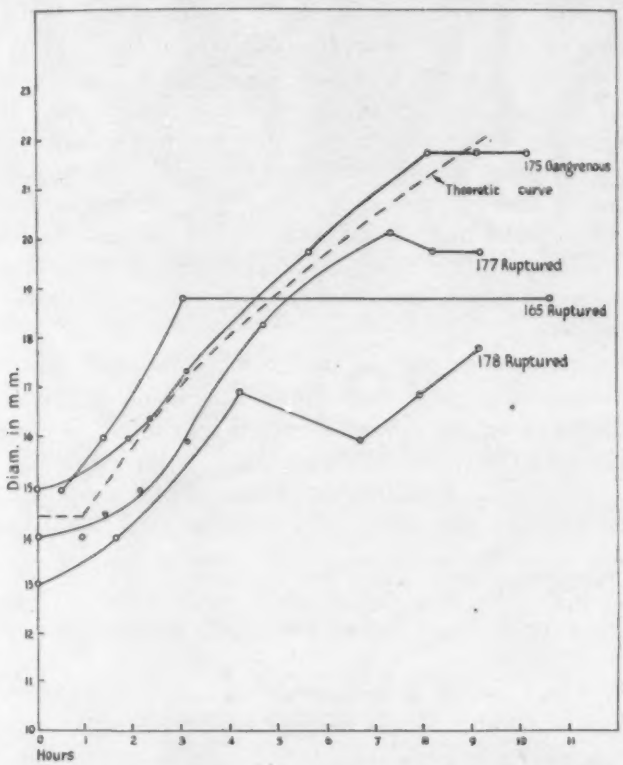

Fig. 5.—Changes in diameter of rabbit cecal appendages after ligation obstruction at the base, measured through a glass window in the abdominal wall. The dotted line indicates the theoretic curve obtained, assuming the rate of volume increase to be constant. The terms "ruptured" and "gangrenous" refer to the findings on laparotomy at the end of the experiment.

Over 50 cc. of fluid was absorbed in five hours. The ligature was removed and the cecostomy closed, the animal being allowed to recover. Four days later the appendage was ligated at the base and incannulated routinely; the pressure rose to 95 cm. in four hours. It is therefore concluded that, although the appendage secretes large amounts of fluid, the cecum absorbs.

VI. *Lack of Effect of Washing the Lumen.*—As it was routine to wash the lumen in order to remove any possible fecal matter which might plug the cannula or the tubing, a series of 7 experiments without preliminary washing was performed, parallel with a second series (of 14) in which each lumen was washed initially with 10 to 20 cc. of 0.9 per cent sodium chloride solution. When experiments of similar duration and with similar pressure were compared, no clear relation was found between cytologic reaction and preliminary washing.

VII. *Influence of Certain Drugs on the Secretion Rate of the Rabbit Cecal Appendage.*—On the assumption that rate of rise in pressure is a measure of the rate of secretion of fluid, the effects of a number of drugs were examined with the aid of the recording manometer. In some cases comparisons were possible with the findings at laparotomy at various intervals after simple ligation and with various time relations between ligation and administration of the drug. In addition, the volume of fluid collected in an intraperitoneal balloon (see the foregoing sections) connected to the obstructed appendage in a given interval after operation and administration of the drug offered a measure of the effect of that drug.

Pitressin, pilocarpine, atropine and epinephrine were studied only in single instances with the recording manometer, and no distinct effect was encountered except for slowing of secretion by 0.5 cc. of epinephrine hydrochloride (1:1,000) given subcutaneously; at the conclusion of this experiment, thirty hours later, the entire mucosa was necrotic. Topical applications of 1 per cent pilocarpine hydrochloride resulted in contraction of the appendical musculature. The effect of doses of magnesium sulfate varying from 0.5 to 2 Gm., given by stomach tube, was explored with the aid of the kymograph in 4 cases, with no conclusive evidence of effect on secretion rate.

Fifteen per cent sodium chloride solution in doses of 0.33 Gm. of salt per kilogram of body weight was injected intravenously because of marked strengthening of peristalis which this medication produces. On the basis of 1 of a total of 3 experiments, it was suggested in the preliminary report [1a] that an accelerating effect might be present. Further kymographic studies, however, show no such effect (fig. 6) as compared to a series of control experiments (fig. 3 *A*); they suggest, on the other hand, a delay of commencement of rise in pressure for one and one-half to two hours. Thirteen rabbits were subjected to simple ligation of the cecal appendage, and the hypertonic saline solution was injected at various times from an hour before ligation to four hours after, the animals being killed at intervals from five to ten hours after operation; the findings were closely parallel to those of control experiments (table 5) except

that serosal tears occurred earlier in the animals treated by injection than in the controls. Experiments with collection of fluid in an intraperitoneal balloon showed no effect from intravenous hypertonic saline solution (table 6).

It was considered that the decrease in time till the serosa tore after intravenous injection of 15 per cent sodium chloride might be due to secretion of some of the excess chloride into the appendix and the passage of fluid with it; however, chloride determinations were made on the fluid from the five, six and seven hour experiments, and the mean values were not altered (499 mg. per hundred cubic centimeters for the controls and 493 mg. for the experimental fluids). Three animals given 25 cc. of 0.9 per cent sodium chloride each at the time of ligation showed serosal tears at five and seven hours and rupture at six hours; in these the mean chloride content was 574 mg. per hundred cubic centimeters, significantly higher than that of the controls (probable error 37 mg.

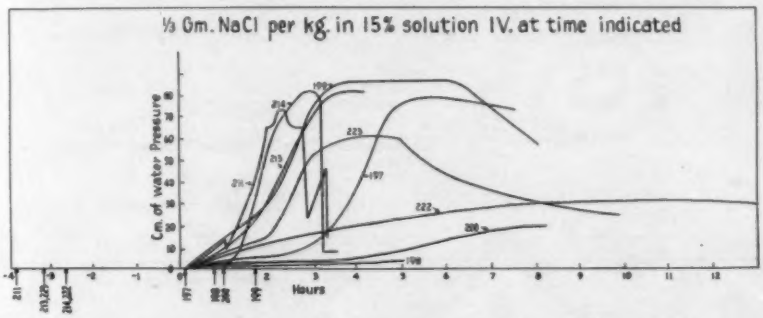

Fig. 6.—Effect of intravenous hypertonic sodium chloride solution on the rate of rise in pressure in the obstructed, incannulated rabbit cecal appendage. (Apparatus: 1 cc. = 100 cm. of water.) The arrows indicate the time of injection (see figure 3 *A*).

per hundred cubic centimeters for experiments with saline solution; and 28.3 mg. per hundred cubic centimeters for controls).

Castor oil in doses of 20 to 30 cc., given by stomach tube, produced no alteration from the result for controls in 1 kymographic experiment or in 4 experiments with simple ligation in which the drug was administered at four and one-half hours and the animals were killed at ten hours, but 5 experiments with the intraperitoneal balloon technic showed that significantly less fluid had been ejected in six to seven hours than in the control experiments (table 6).

In 2 kymographic experiments, croton oil in doses up to 0.2 cc. resulted in an elevation of the rate of secretion slightly above that of any of 8 controls, but 9 animals given 0.1 cc. into the jejunum and subjected to simple ligation presented findings identical with those for the

controls at five, six and seven hours; 4 animals given 0.2 cc. four and one-half hours after ligation presented findings identical with those of controls at ten hours, and, finally, 4 animals given 0.2 cc. at the time of insertion of the balloon and ligation showed ejection of fluid at essentially the same rate as 5 controls (table 6).

TABLE 5.—*Effect of Intravenous Injection of Five Cubic Centimeters of Fifteen per Cent Sodium Chloride Solution on Events After Ligation Obstruction of the Cecal Appendage of the Rabbit*

Duration, Hours	Injection 1 Hr. Before Ligation	Injection at Time of Ligation	Injection 1 Hr. After Ligation	Injection 4½ Hr. After Ligation	Controls	
					A	B
5	Serosal tear	Serosal tear	Gangrene, rupture	.....	Tense	Very tense
6	Serosal tear	Tense and hemorrhagic	Serosal tear	.....	Tense, but no rupture	Tense, grossly acute appendicitis
7	Serosal tear	Serosal tear	Rupture	.....	Serosal tear, rupture, gangrene	Tense
10¼	.....	.....	.....	Acute appendicitis; rupture	Acute appendicitis; rupture	
10¼	.....	.....	.....	Acute appendicitis; rupture	Pale, tense	
10¼	.....	.....	.....	Acute appendicitis; rupture	Acute appendicitis; rupture	
10¼	.....	.....	.....	Acute appendicitis; rupture	Acute appendicitis; rupture	

TABLE 6.—*Effect of Hypertonic Intravenous Saline Solution, Croton Oil and Castor Oil on the Rate of Fluid Ejection by the Ligated Rabbit Cecal Appendage into an Intra-Abdominal Balloon*

	Number of Rabbits	Mean Time Till Rabbit Was Killed, Hours	Mean Volume Collected, Cc.	Minimum Volume Collected, Cc.	Maximum Volume Collected, Cc.
Controls	5	6.3	22.4	17	27
Given 5 cc. of 15% sodium chloride intravenously	5	7.3	24	15	46
Given 0.2 cc. of croton oil	4	8.1	25	17	32
Given 20 cc. of castor oil	5	6.6	15.8	5	24

VIII. *Lack of Effect of Age of Animal on Secretion Rate.*—Four old animals were obtained with considerable difficulty, and the rate of rise in pressure was tested with the apparatus requiring ejection of 1 cc. of fluid for the recording of each 100 cm. of rise in water pressure. Two animals 2 years old and 1 animal 3 years old fell in the high normal range of the controls shown in figure 3 *A* (the controls were animals less than 1 year old; the life span of domestic rabbits is about eight years). In 1 animal, 5 years old, the rate of rise in pressure was

12 cc. per hour, at the lower limit for the controls, but technical difficulties cast doubt on this finding. Microscopic examination of these 4 appendages showed no significant difference in amount of lymphoid tissue from those of younger animals.

IX. *Effect of Appendicostomy on Secretory Rate.*—In 2 animals appendicostomy with delayed (eleventh day) opening of the tip was performed, the fistula thereafter being kept open by cannula. Four days after opening to the outside, the appendages were ligated at the base and incannulated at the tip for kymographic recording. In 1 the curve of pressure rise fell in the center of the control range shown in figure 3*A*; in the other it rose to 48 cm. in four and one-half hours four days after opening of the tip, and to 63 cm. in four and one-half hours seven days after opening of the tip. In both instances it rose more slowly than the slowest of the control group.

TABLE 7.—*Effect of Previous Elevations of Pressure on Rate of Pressure Rise in the Obstructed Rabbit Cecal Appendage*

Pressure Rise No.	Time Required for Rise from 7 to 40 Cm. of Water	Volume Removed from Appendage in Fall from 40 to 7 Cm., Cc.
1	1 hr. 50 min.	5
2	1 hr. 52 min.	5½
3	2 hr. 48 min.	5½
4	5 hr. 56 min.	5
5	Failed	

The final rise was slow, reaching 24 cm. in 4 hours and then falling slowly during 6 more hours. The appendage was found somewhat stretched and also ruptured.

In 2 rabbits appendicostomies were made at the conclusion of recording experiments, the proximal ends remaining obstructed. In both the drainage was watery for two to three weeks and mucoid for another two weeks, after which time the stomas closed completely. With closure, the animals became ill and inactive, one dying two months, and the other two and one-half months, after appendicostomy. At autopsy there was abundant purulent and caseous exudate in the peritoneal cavities of both of these animals; in 1 the appendix could not be found, and in the other it was a necrotic, foul mass. It is evident, therefore, that, although the amount of secretion may decrease somewhat, enough remains to invoke a fatal series of events on closure of the stoma.

X. *Effect of Previous Elevations of Pressure on Rate of Pressure Rise in the Obstructed Rabbit Cecal Appendage.*—Experiments were done on 2 animals to determine the effect of a previous rise in pressure from 7 to 40 cm. of water on the subsequent rises over the same range. For this purpose a siphonage apparatus was arranged which lowered the pressure to 7 cm. automatically after it had reached 40 and measured the volume of fluid removed from the appendage in so doing.

Both experiments showed a slow rise after the second siphonage. One showed at the end that marked stretching of the wall had occurred, and the other showed almost no stretch. The first of these is shown in table 7. Diffuse appendicitis was encountered in each case.

XI. *Effect of Prolonged Pressures at Fixed Levels on Rate of Fluid Production by the Obstructed, Incannulated Rabbit Cecal Appendage.*—It seemed at least equally important to determine the effect of fixed pressures at various levels on the rate of secretion of fluid and incidentally to determine the height of pressure required to incite an inflammatory reaction. For this purpose 5 experiments were

TABLE 8.—*Effect of Prolonged Pressures at Fixed Levels on Rate of Fluid Production by the Obstructed, Incannulated Rabbit Cecal Appendage*

Rabbit	Pressure, Cm. of Water	Decrease in Secretion Rate with Lapse of Time	Duration, Hours	Microscopic Diagnosis
150	5	Yes	67	Serosal appendicitis, grade 1
152	6	Yes	21	Normal *
S20-1	10	Yes	9	Mucosal appendicitis, B1
S20-4	10	Yes	29	Mucosal appendicitis, B1
S20 6	10	Yes	74	Postmortem autolysis
S20-3	10	Yes	23½	Mucosal appendicitis, B3
S20-2	10	Yes	63	Mucosal appendicitis, B4
S20-5	10	Yes	72	Diffuse appendicitis, gr. 1
124	20	No	23	Mucosal appendicitis, B1
149	20	No	46	Mucosal appendicitis, B4 (gangrene, rupture)
160	20	Yes	53½	Mucosal appendicitis, B4
146	23	Yes	25	No section
163	40	Yes	12	Mucosal appendicitis, B1
164	40	Yes	23	Mucosal appendicitis, B4
12 rabbits	40	All Yes	Average 15.2	All grossly acute

* Although the appendage in this experiment showed no changes which fit our classification of appendicitis in the rabbit, there was edema of the mucosal pedicles extending up between the lymphoid villi.

performed with an appropriate kymographic recording apparatus, and 21 additional experiments, planned primarily for collection of fluid at divers pressures (to be reported), provided further data on changes in rate of secretion. The volume measured in such experiments represents the rate of ejection rather than the rate of secretion, the difference being the change in luminal volume due to stretching of the appendical wall. The findings in 1 of the experiments with kymographic recording are presented in figure 4; in this instance the increase in luminal volume was less than 5 cc. (insignificant in comparison to the changes in rate of ejection), and the rate of net transfer of fluid into the appendical lumen therefore decreased with the lapse of time.

The 26 experiments offering evidence in this connection are presented in table 8; all but 2 of this group showed a decrease in rate of secretion with the passage of time. Ten centimeters of sustained intra-

luminal pressure resulted in 4 of 5 cases primarily in infarction of the mucosa; 6 cm. of water pressure led to edema and some disorganization of the mucosa but no change severe enough to fall into our classification, and 5 cm. caused no change. In 12 of the 13 microscopically diagnosed lesions the changes consisted of infarction of the mucosa (mucosal appendicitis, group B) with or without secondary granulocytic invasion.

XII. *Effect of Catharsis at the Time of Rupture on the Course of the Disease.*—In an attempt to test the factor of interference with adhesion formation, 4 rabbits were given 0.2 cc. of croton oil on the tongue, 4 were given 30 cc. of castor oil by gavage and 4 were given 10 cc. of 15 per cent sodium chloride intravenously at the time of simple ligation

TABLE 9.—*Effects of Hypertonic Intravenous Saline Solution, Croton Oil and Castor Oil on Survival of Rabbits After Ligation of the Cecal Appendage*

	Rabbit	Survival Period	Gross Findings
Controls	301	14 days	Rupture; abscess
	304	2 days	Rupture; acute inflammation
	306	2 days	Acute appendicitis; multiple ruptures
	310	7 days	Rupture; abscess
Given 0.2 cc. of croton oil	302	2 days	Rupture; acute appendicitis
	307	17 days	Rupture; abscess
	311	11 days	Rupture; abscess
	315	8 hours	Rupture; acute appendicitis
Given 30 cc. of castor oil	303	10 days	Rupture; abscess
	308	3 days	Rupture; abscess
	312	59 days	Normal appendix
	316	6 hours	Rupture; acute appendicitis
Given 10 cc. of 15% NaCl intravenously	305	Killed at 129 days	Mucocele
	309	11 days	Rupture; abscess
	313	2 days	Rupture; acute appendicitis
	317	67 days	Mucocele

of the true base of the cecal appendage. These medications caused increased numbers of stools but no diarrhea. The average survival period of 4 control animals was six and one-fourth days; the average survival period of those given croton oil was seven and one-half days; that of those given castor oil was eighteen days, and that of 3 of those given hypertonic saline solution was twenty-six and two-thirds days, the fourth being killed at one hundred and twenty-nine days. Of particular interest is the observation that, although the average periods of survival were longer after croton oil or castor oil than in the control group, 1 rabbit of each of these groups given a cathartic survived eight hours or less, a more rapid death than was ever seen in control animals (table 9).

XIII. *Studies Involving Traumatization of the Mucosa.*—Wells [6] has reported a series of experiments concerned with appendicitis in the

6. Wells, A. Q.: Experimental Lesions of the Rabbit's Appendix, Brit. J. Surg. **24**:96, 1937.

rabbit and concluded that obstruction by ligation occasionally results in mucocele formation with masses palpable through the abdominal wall, but "that the only experimental procedure which consistently produced acute appendicitis was obstruction to the lumen of the appendix combined with damage to the mucous membrane." He accomplished that traumatization either by crushing the appendage between the fingers[7] or by transfixing one wall with a needle and scratching the mucosa of the opposite wall. In view of this wide difference of opinion, it seemed worth while to repeat his procedure, also with some variations.

In 2 appendages the walls were rubbed and crushed between the fingers, the wounds were closed and the animals were allowed to awaken. The specimens, removed seven and one-half hours later, showed mucosal appendicitis, group A, grade 3, and diffuse appendicitis, grade 2, respectively.

In order to evaluate the effect of traumatizing the mucosa by scratching with a needle in combination with ligation, a series of 8 rabbits was so treated beside a series of 8 controls, 6 of each being opened at intervals from one hour to two days and 3 being allowed to live till killed by the disease (including 1 opened aseptically at one hour). Although 4 of the control series presented masses palpable through the abdominal wall after eight hours, no masses were to be found in the experimental series. Rupture or leakage through the site of the needle holes occurred in 2 instances, in animals dying at twelve and thirty-eight days, respectively. The microscopic observations were still within normal limits at four hours in the controls, but the traumatized four-hour appendage and all subsequent ones showed advanced changes, with diffuse involvement at the needle holes. The only mucocele in either series occurred in 1 of the animals treated by the Wells technic which died at thirty-eight days, but in the only control rabbit to live for this length of time the appendix could not be found, and caseous exudate abounded in the peritoneal cavity.

In order to be certain that no possible point of difference was being overlooked, the changes in pressure also were investigated by Wells's scratching technic. Five animals were subjected to ligation, scratching of the mucosa, incannulation and pressure recording; in addition, 5 animals were similarly treated except that the mucosa was curetted with a fine bone curet instead of being scratched. The records were within the limits of variability for the controls shown in figure 3 except for 1 of the curretting experiments in which most of the mucosa was removed; only in this case was the rate of rise in pressure slow and the ultimate pressure below that recorded for the controls.

7. Personal communication to the authors.

With regard to mucocele formation, we have been able to produce this condition with simple ligation only if the tie is loosely placed; with this technic mucocele has been produced on each of 5 trials.

For these reasons we find it impossible to corroborate Wells in his opinion that operative trauma to the mucosa as well as ligation obstruction of the lumen is necessary to the development of acute appendicitis in the rabbit.

COMMENT

In the preceding pages it has been shown that the cecal appendage of the rabbit secretes fluid in large amounts and is capable of secreting against a pressure of about 100 cm. of water. When the base is obstructed, the intraluminal pressure is elevated by this outpouring of fluid, and acute appendicitis develops in four to six hours with rupture in eight, the process going on to peritonitis, abscess formation, widespread adhesions and ultimately death of the animal. It has been shown, furthermore, that this process is solely the result of increased pressure, for the same technic without tightening of the obstructing ligature [3] or the same technic with escape of the fluid at 5 cm. of pressure through a cannula placed at the tip did not result in any of these changes but rather in simple low grade serositis from handling the peritoneal cost. The demonstration of Fischer and Kaiserling [8] that the lymphatics from the rabbit cecal appendage run chiefly across the mesentery makes it unlikely that lymphatic obstruction is a factor.

The production of diffuse polymorphonuclear invasion of the appendical wall, with changes fitting into the classification of appendical lesions which can be produced by obstruction alone has been shown to be achievable by direct trauma, but rupture did not occur in the absence of ligation.

In a group of experiments in which the intraluminal pressure was maintained at a constant level, the predominating lesion was found to be infarction and necrosis of the mucosa with varying degrees of granulocytic infiltration. In 1 experiment, in which the pressure was maintained at 6 cm. for twenty-six hours, microscopic examination showed edema and some disruption of the glandular layer without either granulocytic infiltration or actual infarction. Further evidence of the nature of the process is obtained by the use of windows in the abdominal wall; this type of observation demonstrates that the primary change after distention is interference with the blood supply.

In view of the experimental findings which have been discussed in this paper and elsewhere,[3] it is seen that the acute appendicitis following ligation at the base of the cecal appendage of the rabbit must develop

8. Fischer, E., and Kaiserling, H.: Die experimentelle lymphogene allergisch-hyperergische Appendicitis, Virchows Arch. f. path. Anat. **297**:146, 1936.

as follows: Increased intraluminal pressure places tension on the appendical wall with consequent pinching off of some of the vessels and resultant formation of foci of ischemic necrosis, offering a weakened area through which rupture may occur and an open field for whatever bacteria happen to be present. Although Bowers [9] has demonstrated that increased pressure in a sterile hollow viscus can produce granulocytic infiltration, the infiltration in experimental appendicitis in rabbits is probably secondary to bacterial invasion. It has been shown that there is always a greater or smaller number of bacteria in the tissue of the rabbit appendage and that sections from healthy animals often reveal for this reason the presence of a few granulocytes.[2] We have seen rupture occur in the rabbit twelve hours after obstruction without sign of granulocytes when very few bacteria could be found on Gram-stained sections.

That secretion in the true sense of the word, rather than transudation secondary to obstruction of venous circulation, is the decisive factor in the appearance of fluid in the lumen is strongly suggested by the occurrence of this transfer against any level of pressure and by the failure of fluid transfer in two dozen other species investigated.[2]

CONCLUSIONS

1. Simple ligation obstruction of the rabbit cecal appendage results in acute appendicitis presenting all the pathologic manifestations of the human disease.

2. The pressure within the appendical lumen rises after obstruction at the base, and this rise is responsible for the development of appendicitis.

3. The lowest maintained pressure required to initiate the changes characteristic of acute appendicitis is about 10 cm. of water.

4. The rate of fluid secretion is slowed by prolonged pressures at fixed levels.

5. The more advanced the appendicitis, the lower the pressure required to cause rupture of the organ.

6. The effects of various drugs on the rate of secretion of the cecal appendage of the rabbit were tested. None had a marked effect except epinephrine, which stopped the flow.

7. No cathartics studied were found to alter the course of development of acute appendicitis appreciably, but in some instances death was apparently hastened because of inability to localize the infection in the abdomen.

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9. Bowers, W. F.: The Role of Distention in the Genesis of Acute Inflammation of Hollow Viscera, Am. J. M. Sc. **194**:205, 1937.

PAPILLARY CARCINOMA OF THE PELVIS OF THE KIDNEY

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DETROIT

The general facts and clinical details concerning tumors of the pelvis of the kidney are well known. Though such tumors are rare, there have been several reviews of series of cases, and each year there have been isolated case reports reemphasizing this knowledge.

There were apparently 218 cases reported in 1927, and from then until 1932 there were 30 additional cases (Mackenzie and Ratner [1]).

Tumors of the renal pelvis constitute from 1 to 10 per cent of all renal tumors. Five per cent is the average figure usually stated. There are two varieties: the squamous cell tumors, which are the rarer and of which the literature contains only about 60 cases (Higgins [2]), and the papillary tumors, which comprise three fourths of the total number.

The squamous cell growths are the more malignant. They are usually grade 3 or 4 (Broders' classification), are frequently accompanied by stones and chronic inflammation, spread rapidly through the substance of the kidney and are often hopeless, having already metastasized at the time the diagnosis is established. Nephrectomy is the indicated treatment, but no patient has lived five years free from metastasis, and the average duration of life is six to nine months.

By contrast, the papillary growths are the least malignant of all renal tumors (Hunt; [3a] Hunt and Hager [3b]). Gross, sometimes profound hematuria dominates the clinical picture with less emphasis on stones and pyuria. If the growth obstructs the pelvic junction of the ureter,

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From Mercy Hall and Woman's Hospital.

1. Mackenzie, D. W., and Ratner, M.: Tumors of Renal Pelvis: Review of Literature and Report of Case, J. Urol. **28**:405, 1932.

2. Higgins, C. C.: Squamous Cell Carcinoma of Kidney Pelvis, Tr. Am. A. Genito-Urin. Surgeons **30**:13, 1937; Arch. Surg. **38**:224 (Feb.) 1939.

3. (*a*) Hunt, V. C.: Papillary Epithelioma of the Renal Pelvis, J. Urol. **18**: 225-246, 1927; Method of Metastasis of Papillary Epithelioma of the Renal Pelvis, S. Clin. North America **9**:853, 1929. (*b*) Hunt, V. C., and Hager, B. H.: Review of Two Hundred and Seventy-One Cases of Malignant Renal Neoplasms, ibid. **9**:149, 1929.

there is pain from hydronephrosis. Distention of the pelvis of the kidney may produce a large renal tumor.

Pathologically the tumors are usually graded 1 or 1 minus and are analogous to papilloma and papillary carcinoma of the bladder, having the same propensity for spread and reappearance in other portions of the genitourinary tract. Accordingly, one finds in the literature the same discussion of pathologic malignancy or benignancy (Werwath [4]), with the same general conclusion that "microscopic benignancy does not insure innocent behavior" and the warning that the original treatment should be radical.

The tumors spread down the submucosa of the ureter to the bladder. Only at a very late stage are the outer coats of the ureter involved (Kimball and Ferris; [5a] Lower [5b]).

TREATMENT

In 1919, Judd [6] did a nephrectomy with partial ureterectomy for a papillary carcinoma of the pelvis of the kidney. The patient was well for nine months; then there was a recurrence of hematuria, and three or four months later the lower portion of the ureter and the adjacent vesical mucosa were resected. There was a cauliflower-like mass ¾ inch (1.9 cm.) in diameter at the left ureteral meatus. Before Judd's report was published, C. H. Mayo had a patient in whom he fulgurated a papilloma at the ureteral orifice. Three weeks later another attack of severe hematuria called attention to a papilloma in the renal pelvis above. Judd strongly advised resection of the entire ureter with excision of the adjacent portion of the bladder, stating that nothing less radical was sufficient.

Beer [7] in 1921, Hunt [3a] in 1927 and 1929, Kimball and Ferris [5] in 1934, Walters and Braasch [8] in 1935, Smith [9] in 1938 and others have emphasized total resection of the ureter together with a portion of the wall of the bladder as the indicated treatment.

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4. Werwath, K.: Zur Frage der "Gutartigkeit" von Nierenbeckenpapillomen, Zentralbl. f. Chir. **64**:2890, 1937.

5. (*a*) Kimball, F. N., and Ferris, H. W.: Papillomatous Tumors of the Renal Pelvis Associated with Similar Tumors in the Ureter and Bladder: Review of Literature and Report of Two Cases, J. Urol. **31**:257, 1934. (*b*) Lower, W. E.: Neoplasms of the Renal Pelvis with Especial Reference to Transplantation in the Ureter and Bladder, Surg., Gynec. & Obst. **18**:151, 1914.

6. Judd, E. S.: Papillary Tumors of the Pelvis of the Kidney, Journal-Lancet **39**:247, 1919.

7. Beer, E.: Aseptic Nephro-Ureterectemy: Technique and Indications, J. A. M. A. **77**:1176 (Oct. 8) 1921.

8. Walters, W., and Braasch, W. F.: Nephrectomy and Nephro-Ureterectomy for Malignant Tumors of the Kidney, Am. J. Surg. **28**:23, 1935.

9. Smith, G. G.: Surgery of Renal Tumors, J. Urol. **39**:308, 1938.

Nevertheless, in a large proportion of the cases which have since been reported nephrectomy, with or without partial ureterectomy, has been performed. Isolated reports of cases in which nephrectomy was the only treatment still appear (Fritz;[10] Mackenzie[11]).

Kimball and Ferris[5] in 1934 were able to collect 74 cases in which the growth was both in the renal pelvis and in the ureter or the bladder. In 40 of these primary nephrectomy only had been done. There was recurrence in 30. Eighty-six per cent of all recurrences appear in the remaining ureteral stump and in the portion of the bladder adjacent to the ureteral orifices.

After primary nephrectomy for papillary carcinoma of the renal pelvis, with partial amputation of a harmless-looking ureter, there may be an immediate change from a benign to a malignant growth (Judd[6]). Ureters which in ureterograms have shown no evidence of tumor transplants may show extensive growths within a few months after nephrectomy (Smith[9]). Secondary ureterectomy may therefore be difficult because of dense adhesions and infiltration. The growth in the pelvis of the kidney may be small, with early and extensive involvement of the ureter and the bladder (Hinman[11a]). Nevertheless, unless the mass is densely adherent and is hopeless from a surgical or a pathologic point of view, it is always worth doing. In roughly one third of Kimball and Ferris' collected cases secondary ureterectomy was performed with beneficial results.

It is apparently not sufficient to take out the ureter, "funneling out" the intramural portion and closing over the vesical wall at this point, although such a procedure was advocated by Caulk[12] as recently as 1937. The vesical wall for a distance of 1 cm. about the vesical orifice must be excised. The reason is the frequency with which transplants occur at the mouth of the ureter or adjacent to it. Hunt,[3a] Cabot,[13] Beer,[7] Smith[9] and others have stressed the importance of the intramural portion of the ureter. In one third of Hunt's cases "a tuft of tissue was seen projecting from the ureteral orifice and there was definite extension of the lesion to the area of the bladder immediately adjacent to the ureteral orifice." In Cabot and Allen's[14] series, 19 patients on

10. Fritz, L. H.: Papillary Carcinoma of Renal Pelvis, J. Iowa M. Soc. **27**:163, 1937.

11. Mackenzie, D. W.: Papillary Growths of the Renal Pelvis, Canad. M. A. J. **30**:509, 1934.

11a. Hinman, F.: The Principles and Practice of Urology, Philadelphia, W. B. Saunders Company, 1935, p. 1018.

12. Caulk, J. R.: Tumors of the Renal Pelvis and Ureter, Tr. Am. A. Genito-Urin. Surgeons **30**:51, 1937.

13. Cabot, in discussion on Caulk.[12]

14. Cabot, H., and Allen, R. B.: Epithelioma Primary in Renal Pelvis: Report of Forty-Five Cases, Lancet **2**:1301, 1933.

whom total resection of the ureter with segmental resection of the adjacent vesical wall was done had 50 per cent longer postoperative life than 26 on whom nephrectomy and partial ureterectomy were performed. Similarly, Smith [9] noted that in 6 of his 7 cases of ureteral growths there was tumor either in the intramural portion of the ureter or arising from the ureteral meatus.

There have been cases in which the growth repeatedly recurred in the bladder after complete nephrectomy and ureterectomy and the patient was kept alive by repeated fulgurations and segmental resections of the bladder (Patch and Livermore [15]).

The following case report illustrates the benign course of papillary carcinoma of the renal pelvis (duration, ten years), the slow progression down the ureter and bladder and the eventual general metastatic spread of this low grade tumor. Also, the patient received treatment for vesical carcinoma in three hospitals without knowledge that the ureter was still in situ and involved in the tumor. At autopsy the renal pouch and the ureteral bed were still free from cancer, although the abdominal cavity was riddled with it, probably owing to extension via the bladder.

The history of this case has been pieced together from the records of eight admissions to seven Detroit hospitals.

REPORT OF CASE

George A., a man aged 46, was admitted to Mercy Hall on Feb. 2, 1938.

History.—In the summer of 1928, at the age of 38, he had an attack of hematuria. In December there was intermittent abdominal pain. It was not definitely localized but recurred oftenest in the epigastrium, the hypochondrium and the lumbar region, in each instance on the right.

In May 1929 there was hematuria (almost pure blood) accompanied by some distress referable to the bladder.

Examination in the same month revealed cardiac dulness over an area of 2.5 by 10.5 cm. and a blood pressure of 144 systolic and 86 diastolic. The urine gave a 1 plus reaction for albumin and contained 68 white blood cells per high power field and a few red blood cells.

Cystoscopic examination at that time revealed that the vesical urine contained some red blood cells. The first drops from the catheterized right ureter were pure blood; the remainder of the urine was clear.

The dye (phenolsulfonphthalein) did not appear in the right side after fourteen minutes and when it appeared was very pale. On the left side it appeared in three minutes. Three attempts to introduce sodium iodide into the right renal pelvis were only partially successful. Roentgen examination showed a somewhat globular shadow in the right renal area. The diagnosis was tumor of the right kidney.

Nephrectomy was performed on the right side in June. The operation record stated: "The usual lumbar incision was made. The right kidney was somewhat

15. Patch, F. S., and Livermore, G., in discussion on Caulk.[12]

large but appeared normal except that the pelvis was filled with a soft tumor mass. The kidney and pelvis were removed. The pedicle was ligated with no. 2 catgut."

The gross specimen showed "a papillomatous new growth extending from the pelvis upward toward the cortex. The growth extended outside the pelvis as well as within."

Microscopic examination showed "a papillary epithelial new growth of very uniform, not particularly anaplastic, pattern, on a narrow hyalinized stem. There were also some tubular nephrosis and glomerular congestion in the substance of the kidney."

The pathologic diagnosis was "papilloma of the right kidney, grade 1 malignancy."

Fig. 1.—Right kidney (surgical specimen, 1929). The renal pelvis is dilated and filled with a papillary growth derived from the pelvic epithelium. The renal parenchyma is atrophic around the growth but is essentially not invaded by it.

The patient was well for two years after this operation; then he began to pass "clumps of tissue, blood and pus" in the urine. Since 1934 there had been moderate bleeding from the bladder. Since 1935 he had become progressively weaker. His legs became tired easily; he had to rest frequently; there was a choking sensation in his chest and there was dizziness when he arose suddenly.

On April 17, 1936, he was admitted to another hospital. There was evidence of cardiovascular disease (mitral murmur transmitted to the axilla and to the apex 14 cm. from the midline). Papilloma of the bladder was diagnosed, and five radium needles were inserted into the bladder (for twelve hours) through the urethra.

On May 10 the growth in the bladder was fulgurated at still another hospital (the fourth).

On July 17, 1937, cystoscopic examination showed that the tumor which had been fulgurated two months before had disappeared. However, there was a large, compact tumor in the bladder, to the right of the midline, with three or four pea-sized implants on the wall of the bladder.

On August 26 a cystoscopic procedure was done. A specimen removed was diagnosed as carcinoma of the bladder.

On September 25 a suprapubic cystotomy was done at a fifth hospital. A large pedunculated tumor from the left side of the trigon was fulgurated. The pedicle was severed with the electric knife. The remainder of the pedicle was removed to the submucosa, and that area was coagulated.

There was a steady pain down the left leg, unrelieved by change in position.

On October 1 he was admitted to a sixth hospital. The heart was greatly enlarged, and there were marked evidences of hypertensive disease. Cystoscopic study showed three papillary granulomatous masses on the base of the bladder. These were fulgurated. Roentgen study showed diffuse destruction of bone in the left acetabulum and ilium. He was transferred for palliative high voltage roentgen therapy and was discharged from the hospital (the seventh) on December 19.

On his admission to Mercy Hall (the eighth hospital), on Feb. 21, 1938, there were severe backache and pain down the left leg. There was slight pain also in the suprapubic region. Examination showed the patient to be rather stocky, with marked cardiac enlargement and with other evidences of hypertensive disease and rales in the bases of both lungs. The pain in the back increased, as did the hematuria. On March 8 he became drowsy and irrational, had hiccups and gradually sank into coma. He died on March 10.

Summary of Case.—The patient had a low grade papillary carcinoma of the right renal pelvis with onset of symptoms in December 1928, when he was 38 years old.

Nephrectomy with ligation of the pedicle was performed on the right side six months after the onset of symptoms. There was freedom from symptoms for two years; then there were recurrence of the bleeding and appearance of pus in the urine. The patient sought treatment in several institutions. Papillary carcinoma of the bladder was diagnosed cystoscopically and pathologically on three separate occasions during 1936 and 1938, and treatment for carcinoma of the bladder was given on three separate occasions. The patient died on March 10, 1938.

Abstract of Autopsy Report.—Gross Findings: The body was extremely emaciated. The scars of ancient "lower midabdominal," McBurney and "right Mayo kidney" incisions were seen. The entire left lower extremity was enlarged owing to edema. There was only slight edema of the right foot.

When the peritoneal cavity was opened there was observed nodular, firm and conglomerate enlargement of the lymph nodes of the right and left iliac chains, much more extensive on the left than on the right. The nodes were white and partially necrotic. They formed a mass which was partly attached to the bladder and prostate and extended along the aorta to the region of the celiac axis. The vena cava, aorta and iliac vessels were compressed. Metastases to pelvic bones were present.

The lungs revealed irregularly increased consistency due to a nodular type of consolidation. On cut surface the nodules were white to light pink, 3 to 0.5 cm. in diameter, firm and discrete. Portions of the lungs not so involved were emphysematous.

The heart was enlarged, the transverse diameter being increased to 15 cm. Its weight was 600 Gm.

The esophagus was normal, but on the lesser curvature of the stomach, about 8 cm. above the pylorus, there was a superficial ulcer measuring 3 by 5 cm. The remainder of the intestinal tract was normal.

The liver weighed 1,600 Gm. The capsule was generally smooth and glistening, but multiple firm white nodules of varying size were distributed over the surfaces of both lobes. These were from 0.5 to 1.5 cm. in diameter. The cut surface had a

Fig. 2.—Ureters and urinary bladder (postmortem specimen, 1938). Note the papillary growth originating from the mucous membrane of the dilated right ureter, the smooth but dilated left ureter and the papillary growth in the bladder (especially in the region of the trigon and at the top of the fundus). The right renal fossa and the tissues around the ureter revealed no recurrence.

nutmeg appearance and exhibited multiple nodules similar to those on the surface of the liver.

The right kidney was absent. There was no evidence of recurrence in the right renal fossa or in the tissue surrounding the right ureter.

The right ureter was present from its origin in the right renal fossa. It was dilated to 1.5 cm. in diameter and was firm and white. The wall was thickened. When the ureter was opened, milky, thick fluid was observed. The mucous mem-

brane was covered with multiple papillary growths throughout its extent. The growths had not broken through the wall.

The left kidney weighed 240 Gm. Its capsule stripped easily, leaving an irregularly nodular but smooth light red cortical surface in which there were whitish mottled zones of varying size, representing small abscesses. The ureter

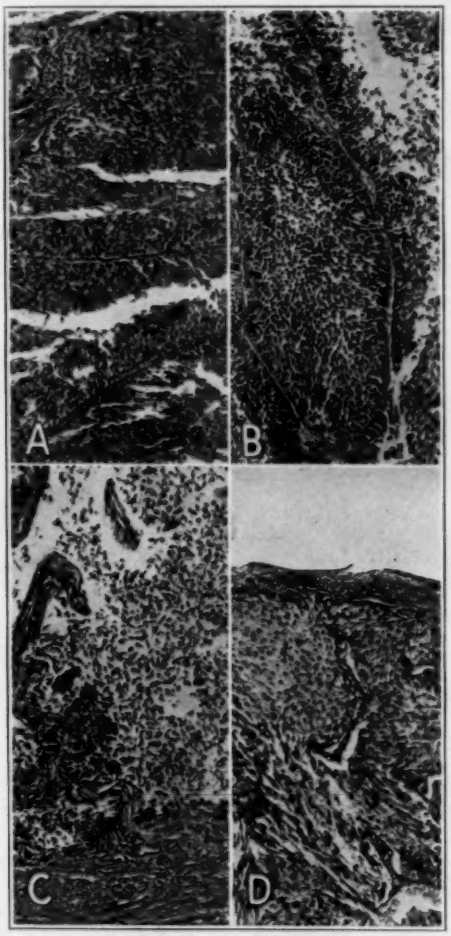

Fig. 3.—*A*, right renal pelvis (surgical specimen) showing the papillary character of the growth. The cells are of the characteristic transitional epithelial type. *B*, urinary bladder revealing the papillary characteristic growth of transitional epithelium (postmortem specimen, nine years later). Note that the degree of malignancy is similar to that observed in the renal pelvis and in the ureter. *C*, papilloma of the right ureter. Many of the cells are exfoliated from postmortem changes. *D*, section of the lung, showing metastasis. Hematoxylin and eosin stain; ×75.

was dilated. It was thin walled and light red and contained turbid urine. The mucous membrane was smooth. It was obstructed in its lower third from the extrinsic pressure of tumor masses in the pelvis.

The bladder was thick walled and contracted. Within the lumen there were only clotted blood and degenerated tissue. The mucous membrane was ulcerated at many points and was transformed into papillary growths of varying size which hung into the lumen. The area of the trigon and the region of the ureteral orifices were ulcerated. Here the usual landmarks were almost destroyed.

The prostate gland was normal. The tissues around the bladder and prostate, especially laterally and posteriorly, were infiltrated with new growth which was continuous with the growths along the iliac vessels.

Microscopic Findings: The tubules and glomeruli of the left kidney were generally hypertrophied. There were also areas of polymorphonuclear neutrophilic infiltration. These involved tubules and other zones, which were sharply circumscribed in the form of abscesses.

The right ureter showed a neoplastic papillary growth of transitional type epithelium extending from the wall into the lumen. The epithelial cells were well differentiated.

The prostate showed chronic pyoprostatitis.

Sections across the ulcer in the stomach revealed the base to be composed of necrotic tissue and pyogenic membrane with fibrosis beneath.

The liver revealed passive congestion of the central venous areas and new growth of transitional type epithelium in local well defined zones.

The bladder revealed areas of ulceration with incrustation, chronic infection and a papillary type of well differentiated transitional epithelial new growth.

The lungs exhibited edema, congestion and nodules of new growth composed of the transitional type of epithelium.

The aortic lymph nodes were involved by metastatic new growth similar to that observed in other metastases.

Anatomic and Microscopic Diagnosis.—The following diagnoses were made:

1. Scar of ancient right nephrectomy (nine years old) for papillary carcinoma of the renal pelvis, grade 2.
2. Metastasis to the right ureter, the urinary bladder, the pelvic and aortic lymph nodes, the liver, the lungs and the pelvic bones.
3. Compensatory hypertrophy of the left kidney (weight, 240 Gm).
4. Obstructive hydronephrosis and hydroureter on the left, with acute pyelonephritis and miliary abscesses.
5. Hypertrophy of the heart (weight, 600 Gm.); hypertension (clinical).
6. Edema and congestion of the lungs with terminal bronchopneumonia.
7. Chronic passive congestion of the liver, with focal and central necrosis.
8. Edema of the legs (pressure of tumor on iliac veins and vena cava).
9. Chronic cystitis and pyoprostatitis.
10. Chronic ulcer of the stomach.

PATHOLOGIC DISCUSSION

In the case presented the chief points of clinical interest as revealed by autopsy were as follows: The patient, who was 46 years old at death, had had a nephrectomy nine years previously for papillary

carcinoma of the right renal pelvis. The ureter had been divided just below the renal pelvis, although the growth was already extensive and had apparently spread beyond the pelvis. At necropsy there was no evidence of local recurrence in the fossa of the right kidney or in the tissue surrounding the right ureter. However, the mucosal lining of the ureter was the site of numerous papillary excrescences extending from the blind upper end to and into the bladder but nowhere breaking through the coats of the ureter. It is probable that the recurrence and extensions came from these malignant papillomas of the right ureter, first extending into the urinary bladder, where multiple malignant papillomas were produced and subsequently involving the regional lymph nodes of the pelvis, the periaortic lymph nodes, the liver and the lungs.

The left kidney was hypertrophied, compensating the loss of the right kidney. The compensatory changes apparently had been adequate until terminal pyelonephritis secondary to obstructive hydroureter, hydronephrosis and encrustation cystitis aided in deciding the fatal outcome. There was also terminal bronchopneumonia.

Also of interest but probably not related to the pathologic changes in the urinary tract was the fact that the patient had cardiac hypertrophy apparently on the basis of severe hypertension, the specific cause of which was not elicited by autopsy.[16] Associated with the cardiac hypertrophy and dilatation there were terminal cardiac decompensation with edema of the lungs and chronic passive congestion of the liver with areas of focal and central necrosis. The pressure of the pelvic tumor mass about the vessels as they entered or came from the left leg was important in producing tremendous swelling of the left lower extremity.

SUMMARY

A case of papillary carcinoma of the pelvis of the right kidney is presented, together with a brief review of the literature.

The significance of the spread of this particular tumor down the ureter and the necessity of complete resection of the ureter at the time of nephrectomy are emphasized.

Several Detroit hospitals at which the patient was treated and several surgeons who treated him permitted the use of their records in the compiling of the data presented.

16. The surgical specimen removed nine years before death showed on microscopic examination "some tubular nephrosis and glomerular congestion in the substance of the kidney."

IMPORTANCE OF SIMPLE ULCER OF THE RIGHT SIDE OF THE COLON IN DIAGNOSIS OF ABDOMINAL DISEASE

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Opportunity to study 6 instances of so-called simple ulcer of the cecum and ascending colon has made evident the seriousness of this relatively rare lesion and the complications which it causes. A knowledge of the attendant symptoms is of especial importance for all those concerned with the diagnosis of abdominal disease, because of the bizarre symptoms, the gravity of the complications which usually ensue and the accompanying high mortality. Direction of attention to the cecum when inflammatory disease of the right lower quadrant of the abdomen is present is especially important whenever the diagnosis of appendicitis is uncertain or the appendix is known to be absent. That the diagnosis is difficult is evident from the fact that it was made correctly before operation in only 1 case reported in the literature.[1] A correct preoperative diagnosis was not made in any of my cases. Nevertheless, familiarity with the condition has convinced me that the diagnosis should be made preoperatively, at least in some instances, and that operation may be better conducted if the surgeon suspects the possibility of such a lesion at the beginning.

The term simple ulcer of the cecum is a misnomer. The condition is not simple in diagnosis or in treatment, and its cause is unknown. Ulcers of the cecum have been called "simple" when they are not associated with tumors, chronic ulcerative colitis, generalized arteriolar disease of the gastrointestinal tract or infection by specific organisms. These specific infections include Endamoeba histolytica, Balantidium coli, actinomycetes, tubercle bacilli and dysentery, typhoid and paratyphoid bacilli. Infection of the intestine and colon by the beta hemolytic streptococcus may result in a suppurative process similar to phlegmonous gastritis.[2] The diagnosis of simple ulcer has been made by the pathologist after exclusion of other conditions of known causation or of other

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1. Bombi, G.: Un caso di ulcera semplica del cieco: Studio clinico e radiologico, Policlinico (sez. prat.) **36**:1550, 1929.

2. Cutler, E. C., and Harrison, J. H.: Phlegmonous Gastritis, Surg., Gynec. & Obst. **70**:234, 1940.

recognized entities. Ulcers for which this term is appropriate, however, resemble one another in most respects, though it is by no means certain that the condition is an entity. In fact, the ulcerations of the cecum associated with uremia (when these are not based on arteriolar disease) bear a strong resemblance to simple cecal ulcers. Both forms are of unknown pathogenesis, but it is to be presumed that the mode of development is different.

Although simple ulcer of the cecum has been known since the time of Cruveilhier,[3] its cause remains entirely unknown. Recent studies have thrown important light, however, on the incidence, clinical features and pathologic anatomy. Among these are the papers of Quénu and Duval,[4] Soupault,[5] Barron,[6] Wise,[7] Wilkie,[8] Bombi [1] and Cameron.[9] Osler [10] mentioned 2 instances of ulcer of the cecum, both with perforation, which were observed by him. A detailed description of these cases did not appear in the literature.

Cameron [9] has pointed out that such ulcers have occurred at ages varying from 18 to 70 years. The condition is twice as common in men as in women. Although he found that a large proportion of the recorded cases have occurred in Scotland and France, my cases from the United States and Sweden, as well as those of others (Barron [6a] and Bombi [1]), indicate that the condition may be encountered over a much wider geographic area. That diet is a factor of uncertain importance is indicated by the fact that some authors [9] have considered such disturbances to be common among persons in whose diet there is a preponderance of cereal grains, and Wilkie [8] expressed the belief that diseases of the cecum have increased with the substitution of meat for vegetables in the diet. There were no unusual dietary habits among the 6 patients whose cases are reported in this paper.

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3. Cruveilhier, J.: Anatomie pathologique: Maladies des intestins, Paris, J. B. Baillière, 1835-1842, vol. 2, pt. 30, plate 3.

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7. Wise, W. D.: Perforating Simple Ulcer of the Colon, Ann. Surg. **93**:1273, 1931.

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9. Cameron, J. R.: Simple Nonspecific Ulcer of the Cecum, Brit. J. Surg. **26**:526, 1939.

10. Osler, W.: Principles and Practice of Medicine, ed. 8, New York, D. Appleton and Company, 1915, p. 521.

Simple ulcer of the cecum usually occurs on the mesial aspect a few centimeters beyond the ileocecal valve. Although several authors have compared this location in relation to the ileum with that of duodenal ulcer in relation to the stomach, there is no sudden chemical alteration in the cecum comparable to that which occurs in the gastric contents when the latter pass into the duodenum. Cameron [9] has stated that the relatively poor blood supply in this region of the cecum may be a predisposing factor. No significant vascular lesions have been found by the pathologist studying these cases. Barron,[6] Bolton [11] and others have concluded that the frequent presence of gastric ulcer in patients who also have ulcer of the cecum means that the two conditions are local manifestations of a general pathologic disturbance and that the same etiologic factor may be the cause of ulcer on any segment of the gastrointestinal tract. Barron [6a] pointed out that simple ulcer may occur on any part of the alimentary tract, from the esophagus to the rectum. The possible neurogenic origin of such lesions has long been a matter of speculation and investigation. The experimental evidence indicating that stimulation of the gastric secretory fibers in the vagus nerves may produce a secretion of gastric juice in the empty stomach and this in turn be followed by acute ulcers [12] suggests that a similar investigation of the lower part of the gastrointestinal tract might be of significance regarding the cause of simple ulcer of the colon.

Study by microscope leaves the nature of the ulcers as much a mystery as does mere inspection. The edges of the ulcers are rather sharp, and there is usually a small amount of connective tissue reaction. Extensive scarring is encountered only in cases of chronic and subacute involvement. Sometimes the edges of the ulcer are almost reactionless. The intestinal wall at the base is thinned even in the absence of perforation. Lymphocytes and polymorphonuclear leukocytes are present about the ulcer, but usually only in moderate numbers. However, in case 4 (this paper) an extensive suppurative reaction was manifested by the presence of many leukocytes and clumps of bacilli and cocci (fig. 3). There are no definite lesions of the adjacent blood vessels. It is unfortunate that there are few studies of the intestinal flora of these patients. There is nothing to suggest a relation to regional ileitis or lymphogranuloma in the present knowledge of the pathology of this lesion. However, if perforation does not occur, one would expect these ulcers either to heal completely or to evolve into a chronic state with accompanying fibrosis and cicatrization. Wilensky [13] has expressed the belief that the granu-

11. Bolton, C.: Ulcer of the Stomach, London, Edward Arnold, 1913, pp. 35-36.

12. Osler, W.: Principles and Practice of Medicine, revised by H. A. Christian, ed. 13, New York, D. Appleton-Century Company, Inc., 1938.

13. Wilensky, A. O.: The Essential Nature of Non-Specific Granulomatous Lesions of the Gastro-Intestinal Tract, Surgery **6**:452, 1939.

lomatous lesions of the intestinal tract represent an end result of intestinal infection marked by secondary or final intramural infection and subsequent attempted overproductive but unsuccessful healing. On the basis of this assumption it has been suggested by Cutler [14] that so-called simple ulcer of the cecum may be an antecedent or initial lesion of cicatrizing enteritis.

The clinical features of simple cecal ulcerations are usually not clearly defined. Cameron [9] could find no really pathognomonic sign. In cases without complications there is usually a history of constipation with occasional melena. There may be vague, dull pain in the lower part of the abdomen, but it is seldom sufficiently characteristic to be of assistance in the diagnosis. One such uncomplicated ulcer of the cecum was excised,[9] the patient making an uneventful recovery. The only preoperative diagnosis of ulcer of the cecum on record was made by studies of the gastrointestinal tract after a barium sulfate enema; resection was performed, and recovery ensued.[1]

Attention is usually directed to simple ulcer of the cecum, however, not by symptoms due to the ulcer itself but by those caused by some complication. Wilkie [8] has reported several cases which are of especial interest because of the variety of complications encountered. In 1, there was moderate hemorrhage. In another, subacute perforation led to pericolitis and the formation of a dense mass resembling a neoplasm. Resection of the cecum was performed, the impression being that the lesion was a true neoplasm; its actual nature was discovered only after the specimen was studied carefully. In a third case, stenosis of the cecum had resulted from cicatricial contraction of adhesions about the base of an old ulcer. A fourth patient had an acute perforation and died of generalized peritonitis. Wilkie [8] also pointed out that a mass resembling an incarcerated hernia may be present in the inguinal region as a result of the slow perforation of a cecal ulcer.

Acute perforation is the most frequent and also the most dangerous complication of simple cecal ulcer. If the ulcer perforates into the peritoneal cavity, rapidly spreading peritonitis inevitably results, usually followed by death. However, Quénu and Duval [4] and Zickler [15] have reported recoveries after prompt closure of the perforation. Perforation of a simple ulcer of the cecum must be differentiated from the other causes of perforation, which may be neoplastic, traumatic, congenital (e. g., a diverticulum) or due to other types of infection. There was a mortality of 57 per cent in the series of 21 instances of perforated cecal ulcer summarized by Cameron.[9] Of the 6 patients on whom operation

14. Cutler, E. C.: Personal communication to the author.

15. Zickler, H.: Ueber einen Fall von Perforation des Colon ascendens, Beitr. z. klin. Chir. **67**:189, 1909.

was not performed, all died; of the 15 patients on whom operation was performed, 9 recovered and 6 died.

A correct diagnosis was made by means of a barium sulfate enema in the case of Bombi's [1] patient, mentioned previously. The preoperative diagnoses which have been made are, in the order of their frequency: appendicitis, peritonitis, cholecystitis, cecal carcinoma, tuberculosis of the cecum, intussusception, intestinal obstruction, subphrenic abscess and postoperative ileus. The signs of perforation of a cecal ulcer could not be differentiated from those of perforation of an acutely inflamed appendix. Christian [12] has stated: "Perinephric and peri-cecal abscess from perforation of ulcer, either simple or cancerous, and circumscribed peritonitis in this region from other causes, rarely can be differentiated until an exploratory incision is made." However, the history may furnish important data which may give a lead as to the correct diagnosis. Whereas perforation of the appendix is always preceded by a period of abdominal discomfort, progressive in severity and often followed by a short period of subsidence of pain, acute perforation of the cecum occurs as a sudden intra-abdominal crisis of excruciating pain located initially in the right lower quadrant. The pain differs from that of perforation of a peptic ulcer only by an early difference in its location and absence of a characteristic history of a preceding gastric or duodenal lesion. Both lesions are always followed by signs of spreading peritonitis. Cholecystitis is less difficult to differentiate on account of its tendency to produce primarily localized symptoms referable to the upper part of the abdomen without evidence of peritonitis. Acute pancreatitis is usually preceded by attacks of indigestion, and a careful history elicits the story of recurrent attacks of milder abdominal pain before the severe crisis occurs. Also, with this disease, pain in the back is often prominent. Intussusception is primarily a disease of childhood and when it occurs in the adult is usually associated with a neoplasm of the bowel. One would not have difficulty in differentiating this lesion from an acute perforation of the bowel, but a slowly progressing chronic perforation of the right side of the colon might easily simulate an intussusception by producing a mass which is brought to the attention of the patient by sudden pain. In considering a diagnosis of tuberculosis of the cecum, one should search carefully for other foci of this infection and remember that every chronic lesion of the cecum and ascending colon is not necessarily due to this disease or to neoplasm. An unnecessarily radical operation might be avoided by this realization and by careful evaluation of all information available before and at operation.

As a perforated duodenal ulcer which drains down the right paravertebral gutter may present prominent symptoms and signs referable

to the right lower abdominal quadrant several hours after the initial attack, attention may be primarily drawn to this region. Again, one must rely on carefully taken history to furnish important differential diagnostic data. Patients with duodenal or gastric ulcer nearly always give a history of digestive upset which may or may not be characteristic of ulcer. Those having primarily ulceration of the lower part of the intestinal tract usually have disturbances of the lower part of the bowel, such as diarrhea, melena or constipation, but not the regular discomfort of peptic ulcer. A plain roentgenogram of the abdomen may show gaseous distention of the cecum and of the terminal portion of the ileum, as in case 1 of this series. The presence of a bubble of gas under the right side of the diaphragm is almost pathognomonic of perforated duodenal ulcer. However, it is quite possible that such a phenomenon might be present with perforation of a cecal ulcer. In case 3 this was true as the result of a subphrenic abscess following perforation of the hepatic flexure of the colon.

It is of especial importance to differentiate a simple ulcer of the cecum with perforation into the retroperitoneal tissues from carcinoma, because of the difference in surgical procedure indicated. Perforations caused by carcinoma are usually slow in onset. The dense scar tissue about a cecal ulcer with subacute perforation may closely simulate carcinoma, as in the case reported by Wilkie.[8] The resemblance is even more complete when bits of intestinal contents escape and become encapsulated on the peritoneal surface. The similarity between these and carcinomatous implants may be striking, as was noted by Sampson.[16]

Differentiation between chronic ulceration of the cecum and ascending colon and regional ileitis may be difficult. The history and results of examination, as in case 4 of the present series, may be similar. Characteristic roentgen findings may be observed in advanced cicatrizing enteritis that establish the diagnosis. However, the final differentation may not be made until laparotomy is performed.

Of the following 6 cases of simple ulcers of the right side of the large bowel, cases 1, 2, 3 and 4 are from the Peter Bent Brigham Hospital. Cases 5 and 6 were contributed in a personal communication by Dr. Clarence Crafoord from the clinic of Dr. Knute Giertz at the Sabbatsberg Sjukhus, Stockholm, Sweden.

REPORT OF CASES

CASE 1.—A physician aged 32 was admitted to the hospital with a diagnosis of right ureteral calculus two hours after the onset of severe pain which radiated from the right lower quadrant of the abdomen to the pubic region. He was doubled

16. Sampson, J. A.: Implantation Peritoneal Carcinomatosis of Ovarian Origin, Am. J. Path. **7**:423, 1931.

up by pain and said that he felt as though "something had burst inside." He was nauseated but did not vomit. In spite of urgency to urinate, he was unable to void.

Four years previously, right renal colic had been relieved after the delivery of a calculus from the right ureter by cystoscopic manipulation. Two years previously, appendectomy had been performed during an episode of pain in the right lower quadrant of the abdomen. It was said that the appendix was mildly inflamed at

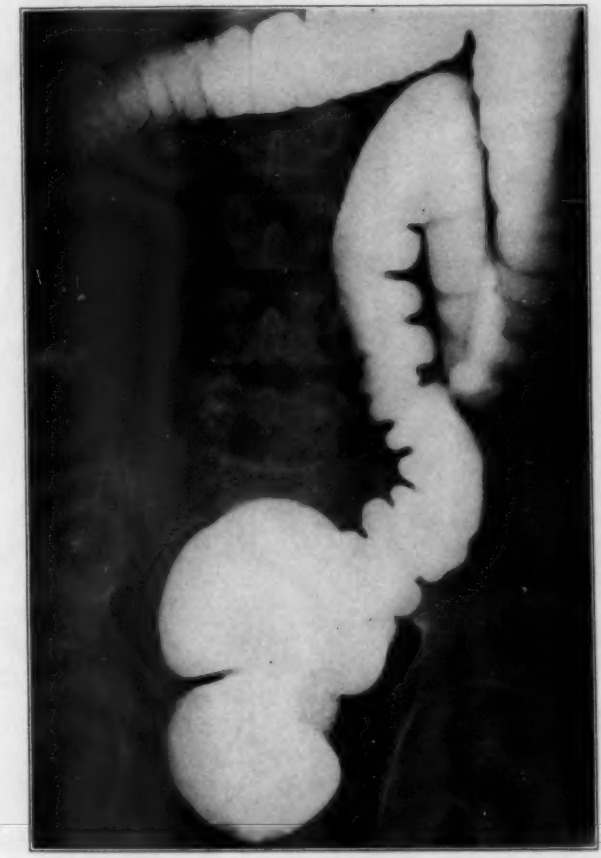

Fig. 1 (case 1).—Results of a barium sulfate enema nine weeks after perforation of the cecum. There is incomplete filling of the cecum and ascending colon. At fluoroscopy there was spasm of the cecum and barium could not be forced through the ileocecal valve.

that time. Two weeks before the present illness he had had an attack of diarrhea and vague abdominal pain, which was thought to be due to food poisoning. After several days the bowel movements became normal, and all discomfort ceased until the onset of the present attack. There was no history of dysentery, but he had been exposed to Balantidium coli during an epidemic in North Carolina.

On physical examination the patient appeared to be in great pain. His temperature was 99.6 F. by rectum. The abdomen showed moderate resistance

in the right lower quadrant, with tenderness at the scar of the McBurney incision. The leukocyte count of the blood was 18,000 per cubic millimeter; 85 per cent of the cells were polymorphonuclears. By catheterization 500 cc. of normal urine was obtained. A roentgenogram of the abdomen showed normal renal shadows. The cecum was distended by gas. During the next hour, signs of peritoneal irritation became definite, with increasing muscular spasm and rebound tenderness always referred to the McBurney scar. The picture was that of perforation of an acutely inflamed appendix, but the appendix had been removed two years before. There was no palpable mass, and peristalsis seemed to be increasing. A diagnosis of early intestinal obstruction due to postoperative adhesions was therefore made, and operation was performed. A right rectus incision liberated a large amount of free purulent fluid from the peritoneal cavity. A smear showed numerous leukocytes but no organisms. The cecum and the terminal portion of the ileum were acutely inflamed, and a considerable amount of fibrin was present over the surface of the former. There was no evidence of intestinal obstruction. When the cecum was lifted, several hundred cubic centimeters of purulent fluid was aspirated from the right iliac fossa. No diverticula were seen or felt. A well healed appendectomy scar was identified. There were no enlarged mesenteric lymph nodes. Three centimeters above the ileocecal valve, on the mesial wall of the cecum, there was an area of acute inflammation surrounded by adherent fat, in the center of which was a hole about 2 mm. in diameter. There was no foreign body present which could have caused perforation. A probe passed gently into this opening entered the lumen of the cecum. There was no palpable mass in the cecal wall suggestive of carcinoma, acute inflammation with slight thickening of the wall being the only demonstrable lesion. The perforation was closed and turned in with two inverting purse string silk sutures. The peritoneum was closed without drainage; the skin and subcutaneous tissues were not sutured. Constant gastric suction was necessary for three days in order to combat intestinal ileus.

Culture of the peritoneal fluid yielded B. coli and a nonhemolytic streptococcus. These organisms were also found in the purulent material from the superficial wound infection. Sulfanilamide was administered for four days after operation. Repeated examinations of the stools showed no amebas or Balantidium coli. Agglutination tests for typhoid, paratyphoid, and Brucella melitensis gave negative results. The temperature did not exceed 101 F., and the patient was well, except for a localized wound infection, three weeks after operation. A barium sulfate enema five weeks later showed spasm and irritability of the cecum; the barium could not be forced through the ileocecal valve (fig. 1). The rest of the colon was normal. A gastrointestinal roentgenographic series made three months after operation showed nothing abnormal. Six months after operation the patient was well and free of symptoms.

Case 2.—A man aged 70 years was admitted to the hospital complaining of urgency and frequency of urination of three years' duration. In addition, a history of repeated gastrointestinal upsets consisting of flatulence, epigastric discomfort and vomiting was obtained. A diagnosis of diverticulosis of the descending colon and sigmoid had been made by means of a barium sulfate enema eight months previously; the cecum appeared normal. At the same time, a gastrointestinal roentgenographic series showed no abnormality of the stomach or of the small intestine. The patient was found to have an enlarged prostate, with retention of urine. After six days of constant drainage of the urinary bladder, a suprapubic prostatectomy

was performed. On the second postoperative day the abdomen became distended, and no gas or fecal material was passed by rectum. In spite of everything that could be done, the abdomen remained "as tight as a drum and silent as a tomb." The patient died on the fifth day after operation. The nonprotein nitrogen of the blood rose to 46 mg. per hundred cubic centimeters and the leukocyte count to 19,000 per cubic millimeter.

At autopsy three chronic gastric ulcers were found near the pyloric end of the stomach. None of these had perforated, and there was no evidence of hemor-

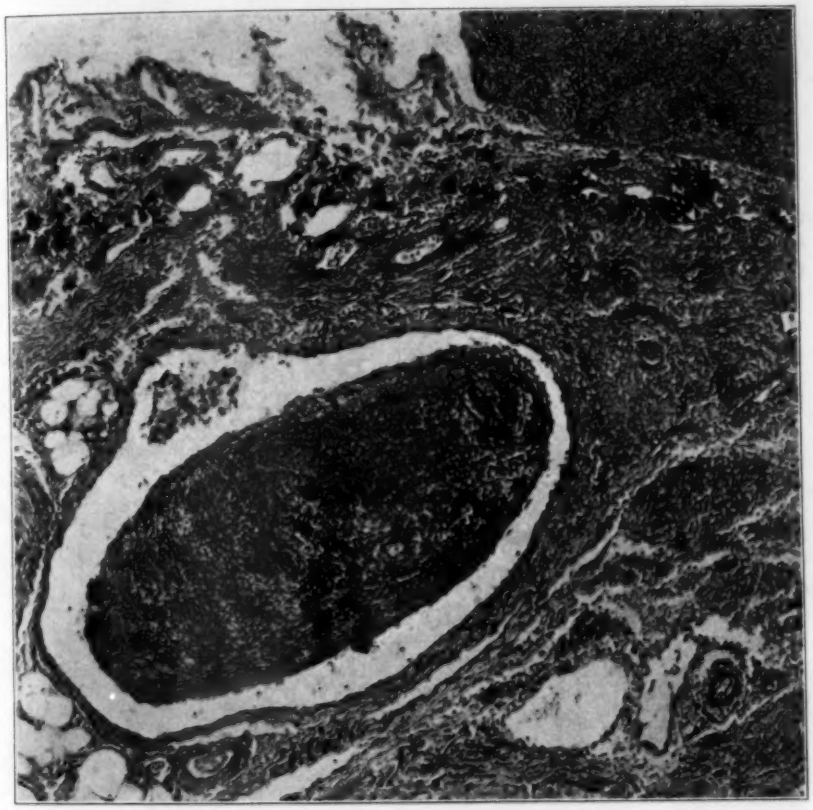

Fig. 2.—Photomicrograph (hematoxylin and eosin stain, × 165) showing an ulcer in the cecum covered by a fibrinopurulent exudate and infiltrated by leukocytes. There is a thrombosed vein in this zone of inflammation.

rhage from them. Six centimeters above the ileocecal valve, lying on the lateral wall of the ascending colon, there was a hemorrhagic and necrotic ulcer 3.5 by 2.5 cm. Its peritoneal surface was covered by necrotic material and fibrinous exudate. About 2 cm. superior and posterior to this ulcer there was a second ulcer, slightly smaller but similar. The entire wall of the upper portion of the cecum and the lower 8 to 10 cm. of the ascending colon were hemorrhagic and friable. The transverse, descending and sigmoid colon showed diverticula which were not inflamed. All the diverticula had demonstrable openings into the colon.

Microscopic examination of sections of the cecum and ascending colon showed extreme inflammation of all layers (fig. 2). There was a fibrinopurulent exudate over the mucosa in some places. The tunica muscularis and serosa were infiltrated with polymorphonuclear leukocytes, lymphocytes and monocytes. Some of the vessels of the submucosa were filled with fibrinous thrombi in the area of inflammation, but this was thought to be a result rather than a cause of the process, since no vessels out of the zone of inflammation were thrombosed. In the regions of ulceration the mucosa and submucosa were absent. The surrounding fat showed infiltration by leukocytes and many bacteria. Fibroblastic proliferation was seen in the cecal wall and surrounding fat. Other sections from the transverse and descending colon showed edema of the serosa and infiltration by leukocytes. A satisfactory explanation of the condition of the cecal wall was not apparent. Amebic infection was not present. The changes were not those of infarction secondary to occlusion of the mesenteric vessels. The patient died as a result of peritonitis secondary to perforation of an ulcer of the cecum.

Case 3.—A man aged 56 years came to the hospital with a diagnosis of right subphrenic abscess and left hemiplegia. For years the patient had suffered from indigestion. Two months previously he had had pneumonia, from which he had not recovered completely. The left hemiplegia occurred during convalescence and led to his entry to the hospital. The patient was pale and poorly nourished. There was no demonstrable motion of the right side of the diaphragm; rales were heard at both pulmonary bases; the heart was moderately enlarged; the abdomen was normal to palpation, and there was flaccid paralysis of the left side of the body. Fluoroscopic examination showed a large bubble of gas beneath the right side of the diaphragm and a fluid level visible near the costal margin. Rib resection and drainage of the subphrenic abscess were performed with the region under local anesthesia. The patient had bronchopneumonia and died twelve days after operation. At autopsy a perforation of the hepatic flexure of the colon was observed. The colon was adherent to the anterior abdominal wall; gas and feces escaped through the opening in the colon into the subphrenic abscess. The perforation was so walled off from the rest of the general peritoneal cavity by the omentum that the intestines remained normal. There was no evidence of ulcerative colitis, diverticula of the colon or carcinoma. The ileum was normal. One could only presume that a primary ulcer of the hepatic flexure had caused the perforation, with subsequent subphrenic abscess and death.

Case 4.—A woman aged 23 years came to the hospital on account of repeated attacks of abdominal pain, nausea, vomiting and diarrhea which had occurred infrequently for two years. However, for two weeks the attacks had been more frequent and more severe and in addition had been accompanied by pain on urination. Forty-eight hours before admission she was awakened by acute epigastric pain and felt violently nauseated. She vomited repeatedly, and diarrhea was severe. There was no hematemesis or melena. The past history was noncontributory. Appendectomy had been performed ten years before.

The temperature was 102.8 F., and the patient was dehydrated. She was in moderate pain but did not appear ill. There was generalized tenderness to deep palpation over the entire abdomen, but no significant localized tenderness and no muscle spasm. There was tenderness in both flanks posteriorly, but neither kidney was palpable. Pelvic examination revealed no abnormality. The leukocyte count of the blood was 14,000 per cubic millimeter, and the catheterized urine contained 15 leukocytes per high power field. Gastric analysis and gastrointestinal roentgenographic series revealed no abnormality. At cystoscopic examination an acute

inflammation of the bladder and a moderate hydronephrosis of the right kidney were found. Cholecystograms showed evidence of a pathologic gallbladder. A barium sulfate enema disclosed a smooth constriction 15 cm. above the ampulla of the rectum. The bowel proximal to this was normal, and a film taken after evacuation showed satisfactory emptying. Examination of the stool showed no blood or pus.

After one week of study, exploratory laparotomy was performed by Dr. John Homans through a right rectus incision. The entire abdominal cavity was explored.

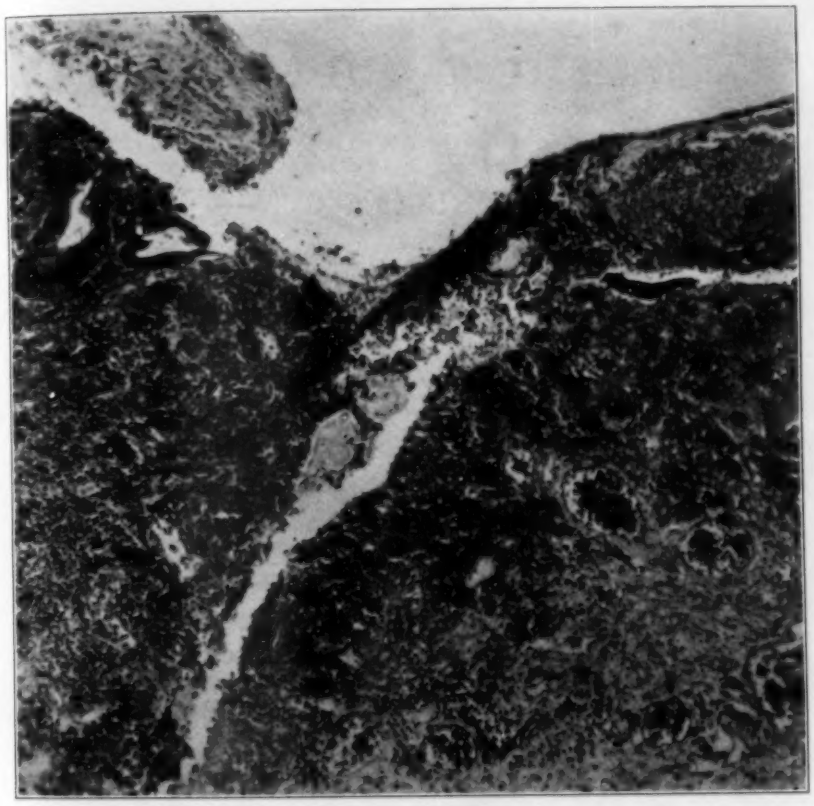

Fig. 3.—Photomicrograph (eosin-methylene blue, × 165) showing an ulcer of the cecum with superficial erosion of the mucosa and a shelving edge of fibrinous exudate. There is extensive infiltration of leukocytes, red cells, fibrin, clumps of bacilli and cocci.

The cecum and ascending colon were covered by adhesions. The ascending colon was bound down just below the hepatic flexure by a mass of old adhesions, which might have been congenital or inflammatory. The bowel was narrowed but not obstructed at this point. The cecum and ascending colon were not reddened, but the wall was thickened. There were several large lymph nodes close to the cecum. The cecum and ascending colon were removed, and an end to side anastomosis of the ileum to the transverse colon was performed. The patient made an uneventful recovery.

The surgical specimen consisted of a resected portion of the ileum 5 cm. long, the cecum and 19 cm. of the ascending colon. There was marked congestion of the serosa, and several injected mesenteric lymph nodes were included. An irregular stellate ulcer measuring 2 cm. in its greatest dimensions was present on the anterior wall of the cecum, just at the ileocecal valve. In the cecum and ascending colon were numerous smaller ulcers, 2 to 4 mm. in diameter. These were covered with a layer of reddish fibrinous exudate. No diverticula were present. Microscopic sections of the cecum (figs. 3 and 4) showed a normal muscle wall and serosa. The

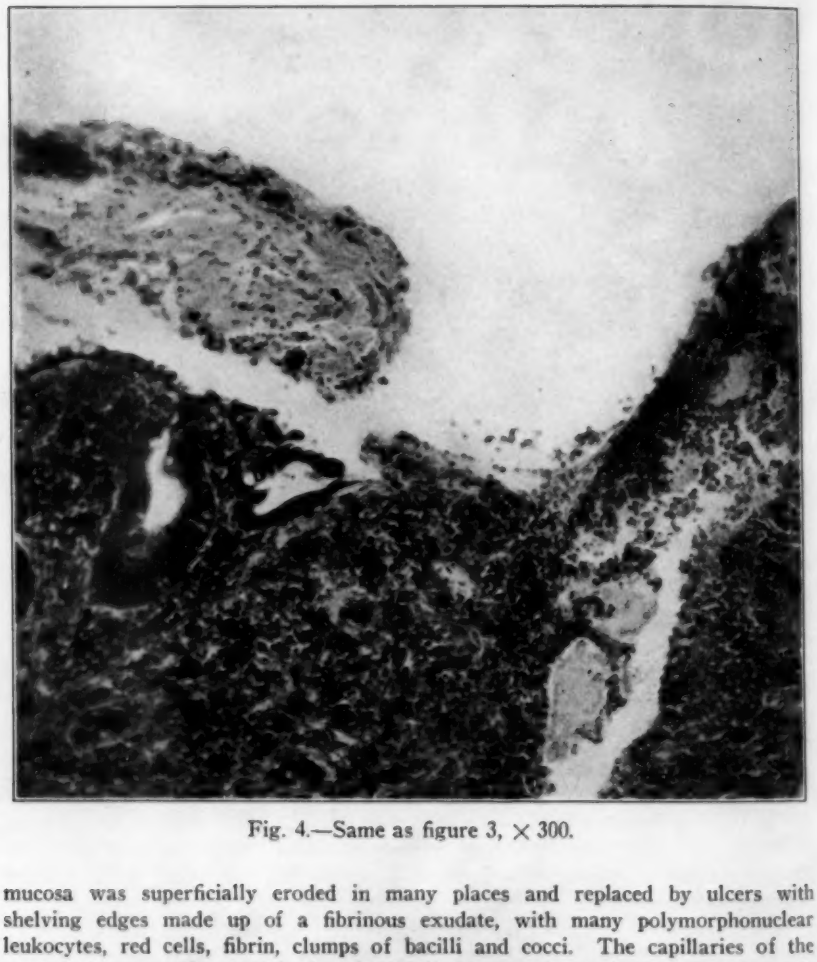

Fig. 4.—Same as figure 3, × 300.

mucosa was superficially eroded in many places and replaced by ulcers with shelving edges made up of a fibrinous exudate, with many polymorphonuclear leukocytes, red cells, fibrin, clumps of bacilli and cocci. The capillaries of the muscularis were dilated. The lymphoid follicles were hyperplastic. The diagnosis was acute ulcerative cecitis, probably bacterial in origin (figs. 3 and 4).

CASE 5.—A woman aged 65 had suffered for several years with vague attacks of abdominal pain and constipation. A roentgenographic diagnosis of gallstones was made, but operation was deemed unwise. Two days before her admission to the hospital, there occurred abdominal pain, nausea and vomiting. When she

was first seen her general condition seemed to be good. The temperature was 38 C., and the pulse was strong. The whole right side of the abdomen was tender, but evidence of peritonitis was lacking. After forty-eight hours of observation, severe acute abdominal pain began on the right side, followed by signs of spreading peritonitis. The patient passed quickly into shock; the skin was cold, clammy and cyanotic. However, after six hours she responded to a transfusion of blood and infusion of saline solution. Operation was performed, and a perforation of the cecum about 5 cm. above the ileocecal valve was found. There was no evidence of tumor or diverticulum. The perforation was sutured and the abdomen closed. The patient died three days later from peritonitis.

CASE 6.—A woman aged 35 suffered from intermittent attacks of diarrhea and constipation for several years. A diagnosis of tuberculosis of the cecum was made by means of a barium sulfate enema. Right colectomy was performed, with end to end ileocolostomy. Pathologic examination showed several ulcers of the cecum and ascending colon with no evidence of tuberculosis, granuloma, typhoid, paratyphoid or dysentery. The patient was later operated on for intestinal obstruction but has since been quite well. The diagnosis by the pathologist was simple ulcer of the cecum.

COMMENT

Perforation of the bowel occurred as a result of the inflammatory process in 4 of the cases in this series. Case 1 was an instance of a sudden intra-abdominal crisis in a young man, due to perforation of the cecum by localized inflammation. Prompt operative closure of the perforation resulted in recovery. In case 4 the patient, a young woman, had repeated attacks of diarrhea, abdominal pain, nausea and vomiting. No abnormalities were demonstrated by roentgen examination, but at operation a definitely abnormal cecum and ascending colon were found, and the resected bowel showed several acute ulcers, probably of bacterial origin. This case is strikingly similar to one reported by Wilkie. In case 6 successful resection of the right side of the colon was carried out by Dr. Crafoord for three simple ulcers which simulated tuberculosis on roentgen examination. In case 5 operation was performed after forty-eight hours' observation, and a perforation of an ulcer of the cecum was closed. The patient was old and succumbed to the peritonitis which had progressed rapidly. In cases 2 and 3 perforation of ulcers of the ascending colon was discovered at postmortem examination.

Roentgenographic barium enema studies were made in 4 of the 6 cases cited here. It is apparent that in the present state of knowledge the correct diagnosis cannot be made by this means of study alone, but it may contribute valuable evidence. In case 1 a barium enema given nine weeks after operative closure of a perforation of the cecum showed persistent spasm and poor filling (fig. 1). In case 2, six months before perforation of the cecum and death, barium studies of the entire gastrointestinal tract had demonstrated no abnormality. In case 4 a barium

enema given several days before operation failed to show evidence of several acute ulcers which were present in the cecum and ascending colon. The roentgenographic diagnosis in case 6 was inflammatory lesion of the cecum, interpreted as being tuberculous in origin.

Owing to the apparent rarity of this disease, little has been learned about it since it was first described, one hundred years ago. As the complications arising from it are attended by such a high mortality, it is imperative that simple ulcer of the cecum be considered in the differential diagnosis of the "acute abdomen." Perforation of such a lesion may simulate perforation of an acutely inflamed appendix or may exhibit a picture closely resembling appendical abscess. Differentiation from a perforated gastric or duodenal ulcer may be difficult. A right rectus incision would usually be the approach of choice. Decision in favor of simple closure of the perforation or resection of the ascending colon can be made only at operation.

SUMMARY

Six patients with simple ulceration of the cecum or ascending colon have been described. The difficulties of clinical diagnosis, the serious nature of the complications of the condition and its wholly unknown etiology and pathogenesis indicate that this kind of intestinal ulceration deserves considerably more investigation than has so far been made.

NOTE.—Since this article was submitted for publication, an interesting case of simple ulcer of the cecum has been published by Moore.[17] In this instance, at operation the lesion was thought to be a neoplasm and resection of the entire ascending colon was carried out. The patient made a satisfactory recovery.

17. Moore, T.: Simple Non-Specific Ulcer of the Ascending Colon, Brit. J. Surg. **27**:600 (Jan.) 1940.

INTRATHORACIC NEUROFIBROMA

A BRIEF REVIEW OF THE LITERATURE AND REPORT OF ONE CASE

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AND
HAZEL R. PRENTICE, M.D.
KALAMAZOO, MICH.

Tumors within the chest are more often discovered now, since the use of roentgen rays has become frequent. During the past few years more attention has been given to these lesions, since the great progress in thoracic surgery has brought about the possibility that benign intrathoracic tumors, particularly, may be successfully approached and removed.

Prior to the use of modern methods of diagnosis of intrathoracic conditions, many tumors were undiagnosed, and only those coming to autopsy were brought to light. Therefore, few benign intrathoracic tumors were correctly diagnosed during life and recorded in the literature.

Of the benign tumors within the chest which have been reported, many were described as originating from nerve tissue elements or structures adjacent to spinal nerves or the sympathetic nervous chain. Although during the past two decades the subject has received more consideration than before, the literature as yet lacks considerable information that undoubtedly would aid in a better understanding. A typical benign intrathoracic tumor is demonstrated in the following case, observed by us:

REPORT OF CASE

M. P., an obese white woman aged 56, was ill for two weeks in March 1939 with influenza. During this illness she had not received the attention of a physician but had remained at her home in bed until the acute symptoms of the disease had subsided. Two weeks after the onset of the illness she presented herself for an examination with the complaints of frequent coughing, weakness, poor appetite, exhaustion on moderate exertion and a dull and somewhat intermittent pain in the right side of the chest in the region of the upper and outer quadrant of the right breast. During the attack of influenza she had had a dry and nonproductive cough, but after a few days transparent, mucoid sputum had been raised, occasionally streaked with bright red blood. Before onset of the influenza she had been in apparently good health and had been able to do her usual housework without any noticeable discomfort except that occasionally she had noticed the dull and intermittent pain in the upper lateral portion of the right side of the chest for about one year. This pain, however, had never been of

great enough intensity to cause her much concern. She had not noticed any pain in the shoulder or the right arm, but at times she thought that she had felt a dull and aching pain at the lower angle of the right scapula. There had been no dyspnea, orthopnea, change in the voice, disturbance in the right eye or the eyelids or sensation of weight or heaviness in the right side of the chest.

Physical Examination.—The height was 5 feet and 5 inches (165 cm.), the weight 196 pounds (89 Kg.), the temperature 98.6 F., the pulse rate 80 and the respiratory rate 22 per minute. The pupils were equal, round and regular and reacted to light and in accommodation. The eyeballs were equally prominent. The eyelids were not abnormal. The neck was short, and there was no engorgement of its veins or visible pulsation of its vessels. The thyroid gland was not palpable. Deviation of the trachea was not noticeable, and a tug was not present. The head moved normally in all directions, and there was no evidence of imbalance of the muscles of the neck. The chest was thick and well padded with fat. Over the anterior part of the chest on both sides the percussion note was resonant. Respiratory sounds were normally heard over the anterior part of the chest, and the voice was not remarkable. The breasts were pendulous but of equal size and free from masses. Examination of the posterior part of the chest revealed relative dulness to percussion over the thick muscles in the upper portion on both sides, and the breath sounds were not as distinctly heard as over the anterior part. The excursion of the lungs at the bases in the posterior part of the chest was apparently normal, and the percussion note was bilaterally resonant over that area. Rales were not heard in any part of the chest. The spine was slightly tender to deep jarring over the thoracic portion, but a definitely localized painful area could not be determined. The heart was in a normal position and without apparent enlargement. The heart sounds were distinct, the rhythm was regular and no murmurs were present. The mediastinal dulness seemed to be within normal limits. The blood pressure in both arms was 140 systolic and 90 diastolic. Examination of the abdomen, rectum, genitalia and extremities revealed no significant findings. A neurologic examination, which included inspection of muscular development and function and tests of the reflexes and sensations was without remarkable findings. The skin was free from lesions and was everywhere smooth and soft.

Roentgen Examination.—A roentgen examination of the chest was advised merely as a routine procedure because of the lack of significant physical findings.

Stereograms of the chest were made. A large mass was present in the upper part of the right side of the thorax. It appeared to extend from the midline well into the upper part of the right side of the chest, involving a considerable portion of the upper lobe of the right lung. The trachea was pushed toward the left but apparently was not compressed to any appreciable degree. The right pulmonary field below the mass and the left pulmonary field appeared clear. There was no evidence of pleural effusion in either thoracic cavity. The border of the mass in the upper part of the right side of the chest was well defined and oval. A lateral roentgenogram of the chest revealed the mass to be in the posterior and upper portion. The bony thorax, the heart and the aorta appeared relatively normal (fig. 1).

Routine Laboratory Examination.—The erythrocyte count was 4,050,000, with 80 per cent hemoglobin, and the leukocyte count 5,800, with 62 per cent neutrophils, 36 per cent lymphocytes and 2 per cent eosinophils. The Kahn test was negative. The urine had a specific gravity of 1.006, an acid reaction and no sugar or albumin: microscopic examination of a catheterized specimen revealed an occasional epithelial cell.

Operation.—About one month later, after the patient's complete recovery from influenza, operation was done (May 19, 1939).

The patient was placed on the table on her left side with the right side uppermost and the right arm extended somewhat above her right shoulder. Intrapharyngeal administration of nitrogen monoxide and ether was used to induce anesthesia. An incision about 9 inches (23 cm.) in length was made between the spine and the medial border of the right scapula in the posterior part of the right side of the chest, beginning about 2 inches (5 cm.) below the level of the spine of the seventh cervical vertebra and curving laterally to a point over the seventh rib. The trapezius and rhomboideus muscles were divided and the right scapula retracted laterally. The second, third and fourth ribs were identified and exposed from the costovertebral junctions to a point slightly beyond their angles. Their periosteum was incised and stripped from them from the costovertebral junction to a point within their respective angles and their freed portion removed. The intercostal muscles were divided and the pleura exposed. Beneath the space thus

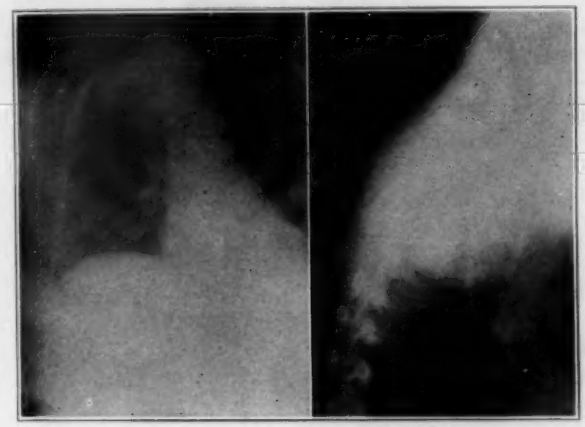

Fig. 1.—Left, roentgenogram showing the large oval shadow in the upper part of the right side of the thorax. The trachea is pushed to the left. Right, lateral roentgenogram, showing the mass in the upper posterior part of the thorax.

made in the upper posterior part of the right side of the chest a stony hard mass could be felt beneath the pleura. It was obvious that the pleura overlying the mass must be incised in order to reach it, and this was done. The mass was completely covered by pleura, which it had pushed well into the right pleural cavity, and compressed the upper lobe of the right lung to a considerable degree. By careful dissection with the gloved hand the mass was easily separated from the lung and was found to be attached by a pedicle about the diameter of a lead pencil to a point opposite the second intervertebral foramen and about 1 inch (2.5 cm.) lateral to it. When the tumor was then divided at its pedicle with the electrocautery there was no active bleeding. Delivery of the mass through the space which had been made by the resection of the portions of the second, third and fourth ribs was not possible, so that the fifth rib was exposed, incised near its costovertebral junction and retracted downward, after which the tumor was easily delivered. Inspection at the site of the attachment of its pedicle revealed that it apparently had originated from structures about 1 inch (2.5 cm.) lateral

to the right second intervertebral foramen. There was no deformity, indentation or erosion of the vertebrae and no evidence that the pedicle of the tumor had penetrated the intervertebral foramen. The right lung, which had not completely collapsed, was reexpanded by positive pressure and the pleura closed with catgut

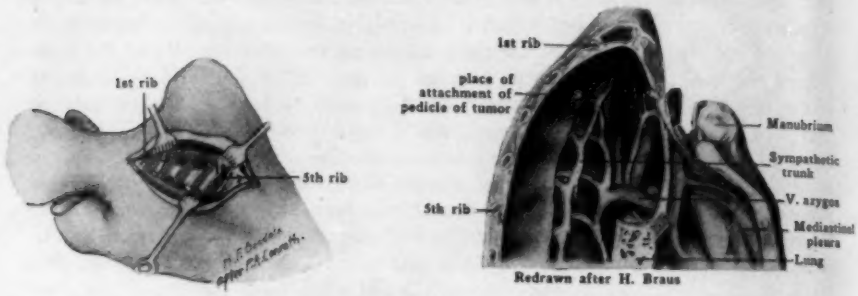

Fig. 2.—Left, diagram showing the position of the wound made. Right, diagram of the relative position of the intrathoracic structures on the right and the point of attachment of the tumor, which has been removed.

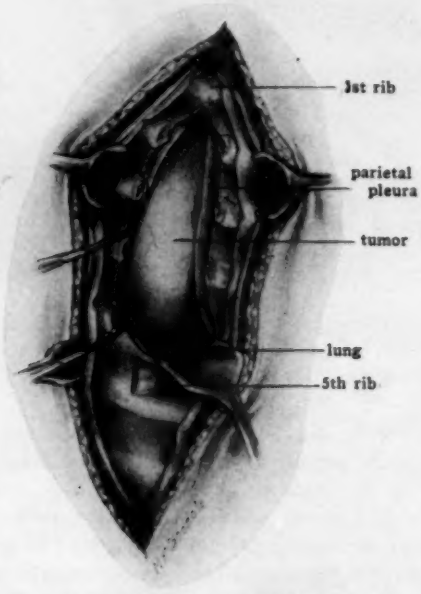

Fig. 3.—Appearance of the tumor on the opening of the posterior parietal pleura.

without difficulty. The remaining wound was closed in layers without drainage, catgut being used for the muscles and interrupted silk sutures for skin (figs. 2 and 3).

Postoperative Course.—Recovery was uneventful, and the patient was discharged from the hospital on the sixteenth day. A roentgen examination of the chest two days before discharge revealed the right lung to be normally expanded, without

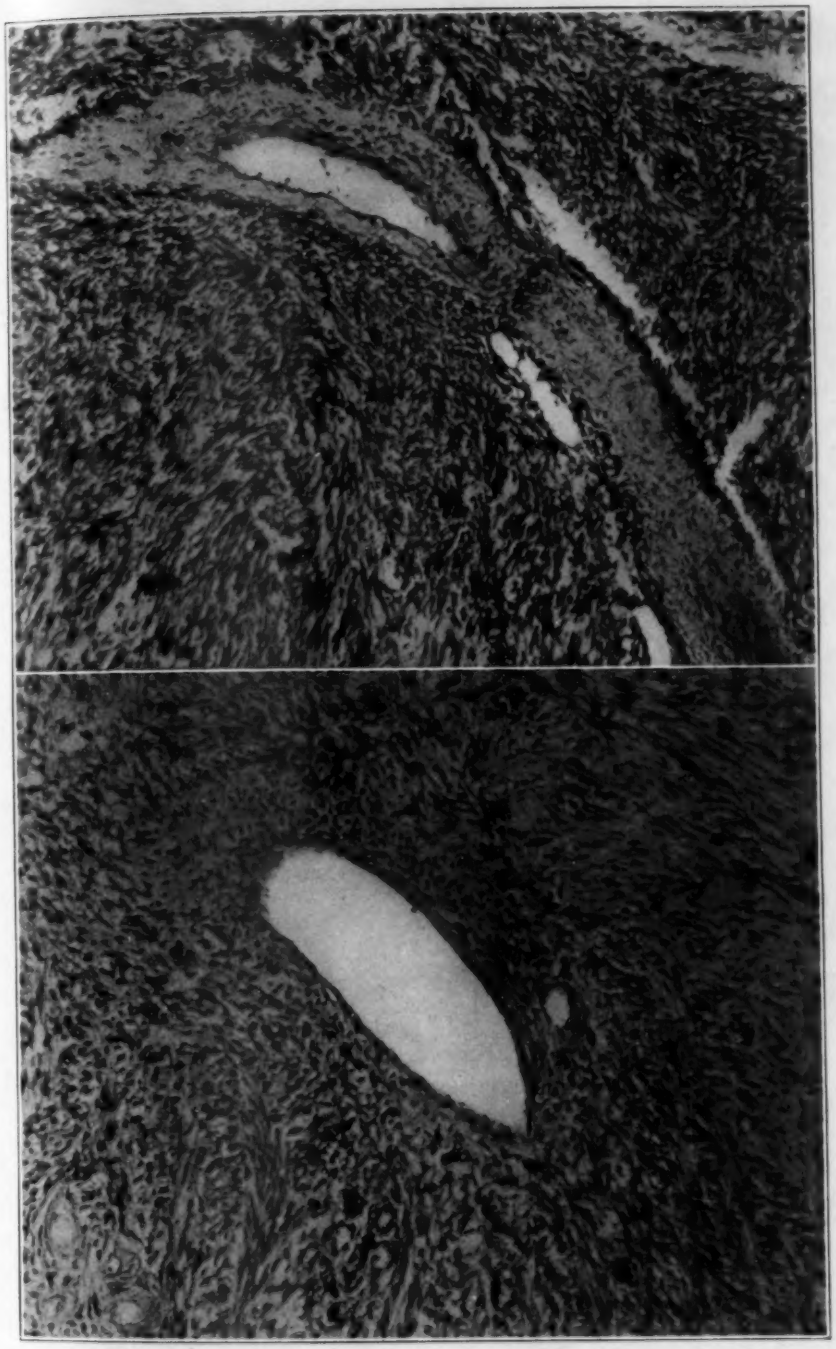

Fig. 4.—Above, photomicrograph of the neurofibroma removed from the upper posterior part of the right side of the chest, showing "palisading" and hyaline thickening of the wall of a blood vessel. Below, photomicrograph of the neurofibroma, demonstrating wavy fibers (right upper corner) and fat-bearing areas around a thin-walled vessel in the left upper corner.

evidence of pleural effusion. The wound had healed by first intention, and dressings were not required after the tenth postoperative day.

Pathologic Picture.—The specimen was examined by Dr. H. R. Prentice, whose report was as follows: "The specimen received was solid, firm, ovoid, 11 by 8 by 6 cm. and well encapsulated. At one pole was a pedicle of connective tissue about 2 cm. across and 0.8 cm. long, which had been severed by cautery. This appeared to arise from the peripheral layers of the capsule and have no gross connection with the tumor."

The cut surface of the tumor was grayish and semitranslucent, with scattered, opaque, yellow areas.

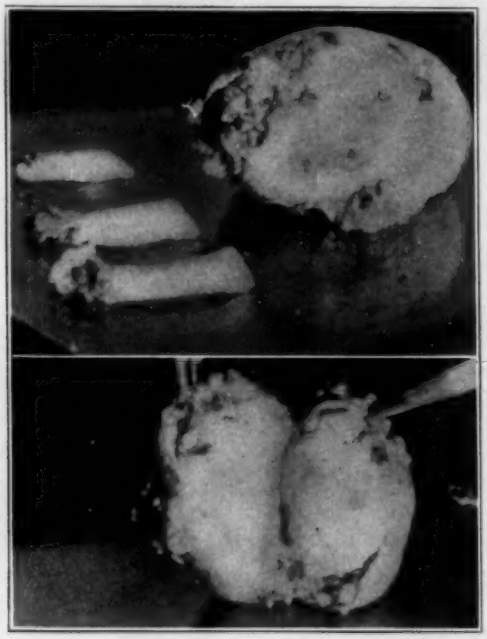

Fig. 5.—Above, gross appearance of the tumor, which measured 11 by 8 by 6 cm., and the resected portions of the second, third and fourth ribs. Below, the tumor cut open to demonstrate the grayish and semitranslucent center and the thick capsule.

Microscopically, the tumor showed partly the slender, wavy fibers and slender nuclei which characterize neurofibromas. In other areas there was a denser structure, with palisading of nuclei, and a tendency to the formation of whorls by cells with nuclei which varied from a slender, elongated form to a plumper form. In some of the plump cells the nuclei were multiple. There were no mitoses. The stroma was vascular, and some of the small vessels showed marked hyaline thickening of their walls (figs. 4 and 5).

The pedicle showed only somewhat edematous connective tissue. There was no evidence of neoplastic invasion.

The general arrangement was orderly, and the tumor was considered benign histologically and in the manner of its growth. It was noted, however, that if removal had not been complete local extension would have had to be feared.

The tumor fell in the class of intrathoracic tumors of neurogenic origin. It had in part the characteristics of neurofibroma—that structure occurring in the grossly white, semitranslucent areas—while in the yellow portions it had the appearance of the tumor which has been variously called neurinoma, perineurial fibroblastoma, lemmoma or schwannoma.

Penfield [1] noted that this combined histologic picture may occur and suggested that perineurial fibroblastoma may occur within a neurofibroma, replacing the tissue of the latter to the edge. Verocay [2] noted that the two types of structure may be associated and suggested the term "neurinofibroma." This is perhaps the best designation for the tumor here examined.

Follow-Up Record.—Three months after her discharge from the hospital the patient was seen and found to be entirely free from the pain in the back and

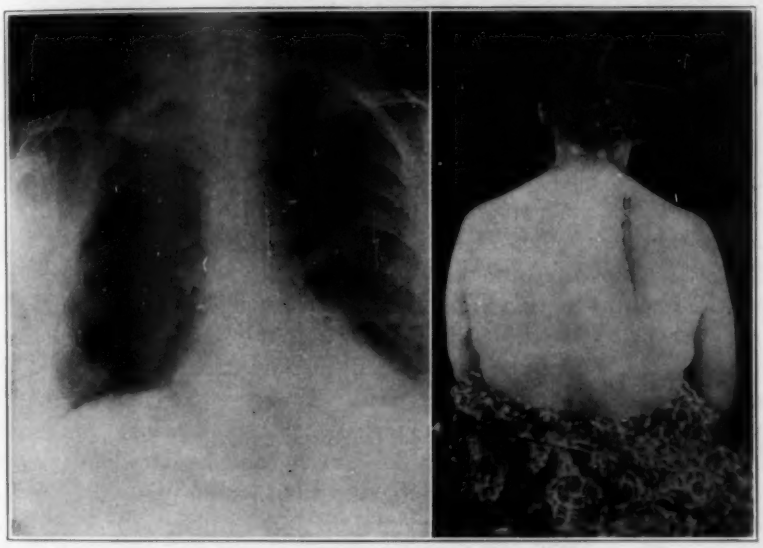

Fig. 6.—Left, roentgenogram of the chest three months after the removal of the tumor, showing normal expansion of the right lung and regeneration of the resected ribs. Right, photograph showing the operative scar.

the right upper and lateral thoracic region. She had regained her normal strength and was able to do her usual housework without discomfort. A roentgenogram of the chest was made at that time and revealed that the right lung was normally expanded and the right pleural cavity clear. The mediastinum appeared normal, and the resected ribs in the upper posterior part of the right side of the chest had regenerated. In January 1940 the patient seemed well and offered no complaints (fig. 6).

1. Penfield, W.: Encapsulated Tumors of the Nervous System, Surg., Gynec. & Obst. **45**:178, 1927.

2. Verocay, cited by Kaufmann, E.: Pathology for Students and Practitioners, translated by S. P. Reimann, Philadelphia, P. Blakiston's Son & Co., 1929, vol. 3, p. 2030.

COMMENT

This case seems to be an excellent one to exemplify how silent a benign thoracic tumor may be, as the condition was discovered only accidentally by roentgen examination. Overholt and Souders [3] recently reported somewhat similar cases (1 case of intrathoracic fibroma and 1 case of ganglioneuroma in younger persons), in 1 of which mild symptoms were apparently present for two years before the thoracic tumor was discovered. Adams [4] stated that physical examination is of little value except when percussion reveals a widened area of dulness in the chest and that diagnosis is made chiefly by fluoroscopic and roentgenologic studies.

The pathologic diagnosis of the tumor in our case is neurofibroma which was located extrapleurally and paravertebrally in the upper part of the right side of the chest. Because of its location and histologic structure it resembles closely the hourglass tumors which have been described by Heuer.[5] The hourglass tumors include a great variety of pathologic conditions, but they arise from a fairly restricted region and pathologically include tumors which most often are neurogenic. Of 64 hourglass tumors which Heuer collected from the literature up to the year 1929, 37 involved the dorsal spinal cord, the thorax or the mediastinum. Six of the tumors were neurofibromas, 5 neurinomas, 5 neuromas, 5 ganglioneuromas and 5 fibrosarcomas, and the remainder of the group limited to the dorsal region included chondrosarcomas, sarcomas and some of which the pathologic diagnosis was uncertain. Heuer found that 5 of the 37 tumors were entirely within the spinal canal, whereas 30 were both paravertebral and within the spinal canal and 2 were paravertebral only. The last 2 occupied the mediastinum and presented a pedicle which entered the intervertebral foramen, but the intraspinal tumor was not sufficiently large to produce symptoms of compression of the spinal cord.

A brief summary of 2 cases (one of Cushing's and one of Guleke's) from Heuer's series follows:

Cushing's Case.—A woman aged 48 for ten years had pain in the right side of the back below the scapula. There were no symptoms of compression of the cord. The patient had point tenderness to the right of the spine at the level of the fifth thoracic vertebra. Roentgen examination showed a rounded mass projecting from the mediastinum toward the right at the level of the second interspace anteriorly and the sixth and seventh ribs posteriorly. There was slight angulation of the dorsal vertebrae at the level of the tumor. Operation was done

3. Overholt, R. H., and Souders, C. R.: Benign Intrathoracic Tumors, S. Clin. North America **17**:905, 1937.

4. Adams, H.: Tumors of the Mediastinum, S. Clin. North America **18**: 629, 1938.

5. Heuer, G. J.: The So-Called Hour-Glass Tumors of the Spine, Arch. Surg. **18**:935 (April) 1929.

in two stages, with approach to the mediastinal tumor from behind. A nodular tumor which was fixed to the side of the vertebral column was removed. It was not positively determined that the tumor did not enter the intervertebral foramen. The patient recovered but continued to have pain in the right side and in the back when she vomited. She was killed five years later in an automobile accident.

Guleke's Case.—A woman aged 33 for five years had a drawing sensation in the right side of the chest and had difficulty in lying on the right side. Infection of the upper part of the respiratory tract associated with a cough and dyspnea developed, which lasted for three weeks and did not entirely clear up. Roentgen examination of the chest revealed a large mass in the right side, which was sharply defined and extended from the fourth to the tenth rib. A large portion of the eighth, ninth and tenth ribs was resected, with marsupialization of the pleura in the first stage, and one month later a large tumor was resected. It was attached by a small pedicle, which disappeared into an intervertebral foramen. The patient recovered after postoperative development of empyema and was in good condition four months after operation.

The structure of our tumor, as of the hourglass tumor, indicated that the origin was probably from a spinal nerve or the fibrous structures, ligaments or periosteum within or near the intervertebral foramen of a spinal nerve.

Harrington [6] studied 46 intrathoracic tumors, of which 11 were proved to be neurofibromas on microscopic examination. Ten of these were situated in the posterior mediastinum, whereas the other was on the left thoracic wall along the course of the ninth intercostal nerve. A brief summary of 1 of Harrington's cases, which closely resembles our case, is as follows:

Harrington's Case.—A woman aged 53 had pains in both sides of the chest on coughing and on deep breathing. Physical examination gave essentially negative results. Roentgen examination of the chest showed a shadow in the right side of the mediastinum at the level of the fourth and fifth ribs. At operation the approach was posterior, through a space made by the resection of the fourth and fifth ribs. The tumor was situated in the upper posterior part of the right side of the mediastinum, to the right of the aorta, and at the level of the third intercostal space it was attached to the body of the vertebra. This patient made an uneventful recovery and was discharged from the hospital on the twenty-eighth postoperative day.

Overholt and Souders [3] in 1937 grouped the benign intrathoracic tumors as follows: (1) dermoids and teratomas; (2) fibromas, neurofibromas, perineurial fibroblastomas and ganglioneuromas; (3) osteomas, chondromas and osteochondromas; (4) myxomas; (5) lipomas, and (6) hemangiomas, cystic hygromas and lymphangiomas. They expressed the opinion that the most numerous and the most important of these groups are the first two. They stated:

[The tumors of the second group] are . . . found posteriorly in the thorax, . . . along the gutter between the ribs and the vertebrae, adjacent to

6. Harrington, S. W.: Surgical Treatment in Fourteen Cases of Mediastinal or Intrathoracic Perineural Fibroblastoma, J. Thoracic Surg. **3**:590, 1934.

the sympathetic nerve chain. Occasionally they approach the intervertebral foramina and sometimes grow through this opening into the spinal canal when they assume the dumb-bell shape and are prone to cause neurologic symptoms. . . .

These are among the most silent tumors in the thorax and some cause no symptoms whatever.

Solitary neurofibromas have been less commonly encountered within the thorax than within the skull, where they are frequently attached to the acoustic, optic or trigeminal nerve, or within the spinal canal, where the point of origin is usually a posterior root.

Penfield [1] explained that the solitary neurofibroma or perineurial fibroblastoma is an encapsulated tumor attached to a spinal nerve root or to a cranial nerve and is centrally located, whereas the neurofibromas of von Recklinghausen are usually multiple and involve the peripheral nerves. In the differentiation of the solitary neurofibroma and the multiple neurofibromas of von Recklinghausen's disease it must be remembered that the origin of the tumors is essentially the same, in that the growths seem to arise

from the specialized investment which separates and insulates nervous tissue from the rest of the body. . . .

The multiple superficial tumors which appear in neurofibromatosis are an expression of a system disease. . . . The condition shows marked hereditary tendencies. . . .

The tumors of [neurofibromatosis] . . . represent a . . . thickening . . . [of the nerves due to] a congenital abnormality in the structure of the peripheral nervous system. . . .

Fibers of the nerve enter the tumor at one end and leave it at the other. . . . [there being a] connective tissue increase about the fibers of the nerve. . . .

Because of this . . . intermixture of nerve fibers with connective tissue, the . . . term *neurofibroma* [indicates] *fibroma* on and in a nerve. . . . In solitary perineurial fibroblastomata the . . . normal nerve is . . . applied to the capsule of the tumor without penetrating it.

Andrus,[7] in tracing the derivation of various elements composing the nerves and ganglions of the thorax, pointed out that neurofibroma is "a tumor arising from a nerve and containing any or all of the constituents of the nerve trunk. Such tumors are thought to spring . . . from the perineurial or endoneurial . . . tissue."

Tumors may present themselves in many locations in the chest. However, neurogenic tumors obviously occur most often in the posterior thorax. For this reason, they are probably best approached operatively through the back of the chest. If there are symptoms of compression of the cord it is advisable to attack them by laminectomy, with the idea in mind that both the intraspinal portion and the intrathoracic portion of the tumor may be removed by the extension of the one incision.

7. Andrus, W. DeW.: Tumors of the Chest Derived from Elements of the Nervous System, J. Thoracic Surg. **6**:381, 1937.

When there are no symptoms of involvement of the spinal cord, it seems to be less hazardous and wiser to use the thoracic approach. Each individual case is a problem in itself, and the decision must be based on this fact. Harrington advised that pneumothorax should be induced three to five days preoperatively to adapt the patient to an open pneumothorax during the operation.

Benign intrathoracic tumors, although less frequently seen, are relatively more important than the malignant growths, because successful removal and cure are possible. When they are discovered within the chest, because of the frequency of their position in the upper and posterior portion of the thorax, the surgical approach and exposure need not be too difficult. A complete extirpation may be the rule rather than the exception, and the postoperative course, even in elderly patients, may be essentially uneventful. Early and complete removal of such tumors is of the greatest importance, not only because their gradual enlargement may result in serious pressure within the thorax but also because of the possibility of sarcomatous degeneration, which has been proved to occur.

SUMMARY

1. A case of intrathoracic neurofibroma is reported in which the growth was discovered accidentally by roentgen examination in a woman aged 56.

2. A favorable surgical approach to benign lesions of the upper posterior part of the thorax is described in detail.

3. The incidence and pathologic picture of intrathoracic neurofibroma are briefly reviewed and discussed.

4. The prognosis for surgical treatment is debated.

INFLUENCE OF BONE ASH ON THE REPAIR OF BONE

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In a previous publication [1] there was presented experimental evidence that bone ash aided ossification. In the reported experiments transplants of osteogenic tissue were cultured in the anterior chamber of the eye in a medium saturated with bone ash. It was suggested that the minerals used in the formation of bone exist in bone and in bone ash in a physicochemical form particularly suitable for use in the process of ossification.

To examine this evidence further, the influence of bone ash on the repair of fractures was investigated in a series of 11 rabbits. In the original series of 24, 13 were lost by death or infection.

METHOD

In each animal equal segments were removed from the shaft of each radius in total block resection, and to discourage repair small bits of costal cartilage were placed in the defects between the fragments. In addition to cartilage, bone ash derived from bones of other rabbits was used to fill the defect in each right radius. The left one contained only cartilage and served as a control for comparison. The process of repair was followed by means of weekly roentgenograms over a period of four weeks and examined post mortem at the end of this period.

RESULTS

There was failure of repair of 3 of the defects which contained bone ash and of only 1 of the controls. In most instances the callus which formed in the presence of bone ash was larger but less well defined and organized. Microscopically, in the specimens in which many particles of the ashed bone were still present there was some residual inflammatory reaction around and within the site of repair.

From the Departments of Physiology and Surgery of the University of Nebraska College of Medicine.

1. Bisgard, J. D.: Ossification: Influence of Mineral Constituents of Bone, Arch. Surg. **33**:926-939 (Dec.) 1936.

Fig. 1.—Roentgenograms of the radiuses of a rabbit. *A*, the day after the operation. Note bone ash in the defect in the right radius. *B*, four weeks later. Both defects have been repaired and there is firm union between the fragments. Note in *B* considerable bone ash and excessive callus in the right radius.

Fig. 2.—The radiuses of another rabbit. *A*, the day after the operation and *B*, four weeks later. Although both defects are well repaired, the left one, which had no bone ash, repaired more normally.

Fig. 3.—Roentgenograms of a rabbit in which there was failure of repair of the defect in the right radius, the one containing bone ash. In the left radius, the control, the defect repaired normally. *A*, the first, and *B*, the final, roentgenogram.

Fig. 4.—As in the rabbit of figure 3, so in the one shown in these roentgenograms: normal repair of the defect in the control radius and failure in the one containing bone ash. *A*, the earliest roentgenogram; *B*, the final roentgenogram.

In figures 1, 2, 3 and 4 are illustrated the first and last roentgenographic records of 4 representative animals.

CONCLUSION

From these experimental data there is no evidence that bone ash aids the repair of bone. On the contrary, the evidence indicates that it may have a deleterious effect.

ADENOSQUAMOUS CARCINOMA OF THE PERIPAPILLARY PORTION OF THE DUODENUM

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AND
DAVID R. MORGAN, M.D.
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Adenosquamous and squamous carcinomas of the duodenum are exceedingly rare lesions, only 5 cases, 3 of the former and 2 of the latter, having been reported in the literature. Three of the growths were peripapillary, and the others were localized in the suprapapillary segment of the duodenum. One of these involved the common bile duct by extension. The purpose of this communication is to review the essential features of these cases and to record an additional example of adenosquamous carcinoma of the peripapillary portion of the duodenum.

REPORT OF A CASE

H. C., a white man aged 49 years, entered the Elk County General Hospital, Ridgway, Pa., on Feb. 24, 1932, with jaundice, fever and moderately severe epigastric pain of short duration. Roentgenograms showed what was interpreted as a defect, probably neoplastic, of the pyloric portion of the stomach. The symptoms subsided, and the patient returned to work at the end of two weeks. After a short interval jaundice reappeared, in association with clay-colored stools and dark urine. Subsequent complaints were eructations and a sense of abdominal distention after meals, accompanied by pain in the upper portion of the abdomen. The pain was severe at times but did not radiate. There was no vomiting, and the appetite remained good, yet the patient lost 40 pounds (18 Kg.) during a period of three months. Roentgenographic examination was repeated on April 2 but showed no gastric defect; changes were observed in the gallbladder which suggested a neoplastic process.

Physical Examination.—The patient entered Jefferson Hospital on June 22 because of marked generalized itching. Examination showed a well nourished, deeply jaundiced subject. The liver was palpable 8 cm. below the costal margin in the midclavicular line. It was moderately firm, tender and movable. No other masses were seen or felt, and there was no evidence of free fluid in the peritoneal cavity.

Laboratory Data.—Roentgenograms of the gastrointestinal tract suggested the presence of an extraintestinal lesion in the upper portion of the abdomen, which

From the Pathological Laboratories of the Jefferson Medical College and Hospital, and the Department of Neoplastic Diseases.

was interpreted as a pancreatic lesion, an enlargement of the liver or a new growth. A small amount of barium sulfate remained in the stomach at the end of six hours, indicating delayed emptying. The hemoglobin content of the blood was 62 per cent, the red cell count 3,690,000, the color index 0.84 and the white cell count 8,600 (polymorphonuclear neutrophils, 86 per cent). The urine was acid, brown to black, with a specific gravity of 1.010 to 1.016, a trace of albumin and occasional epithelial cells. It contained no sugar, no blood and no casts. The gastric contents showed a residual total acidity of 28, but no free hydrochloric acid; after a test meal these figures gradually rose to a maximum of 62 and 41 respectively at the end of forty-five minutes. Blood was present in the last gastric specimen, and lactic acid and bile were absent from all specimens. The stools were well formed, grayish brown and alkaline, and contained blood and considerable quantities of mucus, but no ova, no parasites and no excess of fats. The van den Bergh reaction was positive, biphasic, and the serum bilirubin was 11 mg.; 80 per cent and 90 per cent respectively of bromsulphalein (2 mg. dose) was retained at the end of thirty minutes on two occasions. The nonprotein nitrogen content of the blood was 34.32 mg. per hundred cubic centimeters of blood. The Wassermann reaction of the blood serum was negative.

Course.—At laparotomy on August 2 a greatly distended gallbladder was exposed, and 50 cc. of white bile was aspirated. Palpation did not reveal the exact cause of biliary obstruction, which, however, was thought to be in the common bile duct. An anastomosis was established between the gallbladder and the stomach. Bleeding appeared postoperatively; the temperature rose from 96 to 106 F. and the pulse rate from 60 to 120 per minute. The patient died the following day.

Postmortem Examination.—Autopsy was performed eighteen hours after death and was limited to the abdomen. The combined gross and microscopic diagnoses were: (1) adenosquamous carcinoma in the region of the papilla of Vater with obstruction to the common bile duct, hydrohepatosis and marked jaundice; (2) surgical cholecystogastrostomy; (3) chronic cholecystitis; (4) biliary cirrhosis of the liver; (5) hemoperitoneum; (6) cholemic nephrosis, and (7) bronchopneumonia.

Gross Examination: The peritoneal cavity contained a large amount of liquid and clotted blood. The serosa was everywhere smooth and glistening, and the operative wound was clean. The kidneys, weighing 200 Gm. each, were deeply jaundiced, and the cortex was markedly swollen.

The common bile duct and the cystic and hepatic ducts were considerably enlarged, the distention reaching into the finer intrahepatic radicles of the biliary system. The papilla of Vater was prominent, and the ring of tissue about its stoma was firm and fibrous-like. The pancreatic duct was not explored. Adjacent to the common bile duct, between it and the vena cava, was a lymph node the size of a lima bean. The gallbladder was distended with blood, and its wall was slightly thickened. A considerable quantity of blood and coffee ground flocculi were present in the stomach and duodenum. The liver, weighing 3,290 Gm., was soft, smooth and green, and section disclosed marked distention of the intrahepatic biliary ducts.

Microscopic Examination: One section of the duodenum included the terminal segment of the common bile duct.[1] The wall of the duct was thickened by chronic inflammatory tissue, and the surface epithelium was partially autolyzed and desquamated. Approximately 0.5 cm. from the termination of the common duct in the duodenum, a neoplastic growth was observed on the surface (fig. 1). On

1. This is known both as the ampulla of Vater and as the common bile duct, but in this communication it will be called by the latter designation.

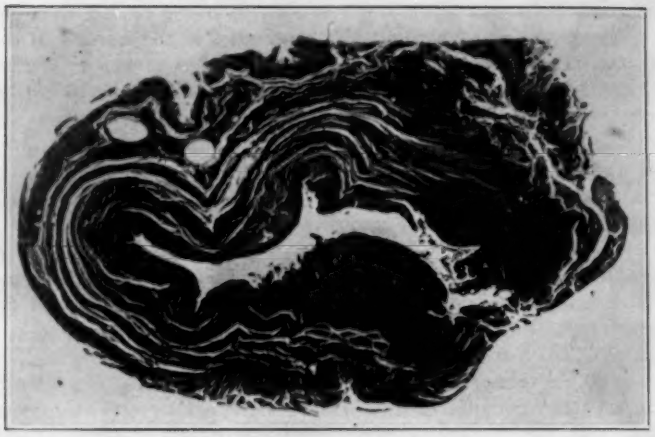

Fig. 1.—Terminal end of the common bile duct, which is surrounded over a greater portion of its circumference by the duodenal mucous membrane. At the lower right is the orifice of the duct, and just behind this on each side are the nodular neoplastic excrescences (× 15).

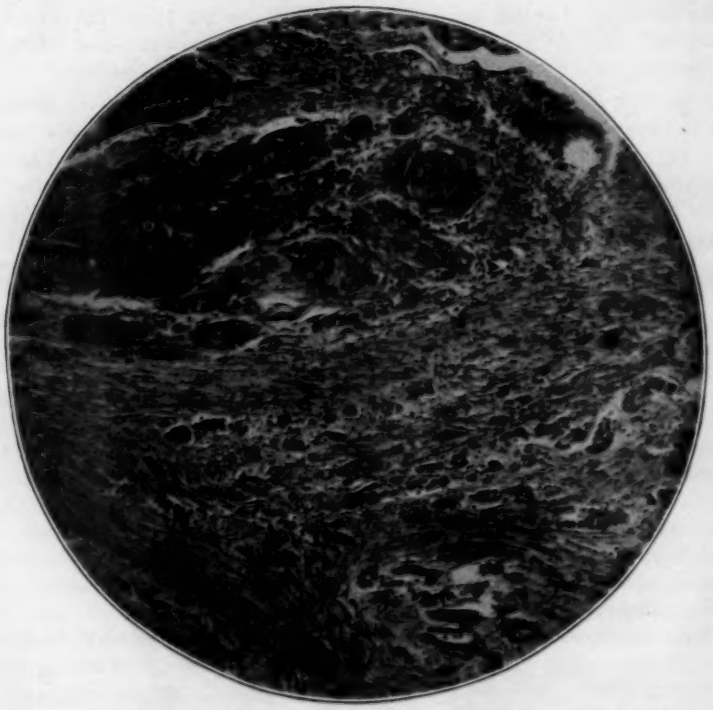

Fig. 2.—Intraduodenal segment of the wall of the common bile duct, showing epidermoid differentiation with pearl formation above and glandular differentiation below. Details are well brought out with the aid of a hand lens (× 100).

one side this consisted of a flat plaque of infiltrating glandular epithelium arranged as acini, cords, nests and masses and, adjacent to this, a nodular villous projection composed of undifferentiated cells, epithelial pearls and acinous structures (figs. 2 and 3). On the opposite side of the duct was an area of ulceration bordered by infiltrating, well differentiated epidermoid carcinomatous tissue. The duodenal mucous membrane surrounding the orifice of the common duct was somewhat autolyzed. Its deeper portion was infiltrated with tumor cells of the squamous and the glandular type (figs. 4 and 5).

A second histologic section of the duodenum included a small wedge of fibrotic pancreatic tissue, an intramural segment of the duct of Wirsung and, externally,

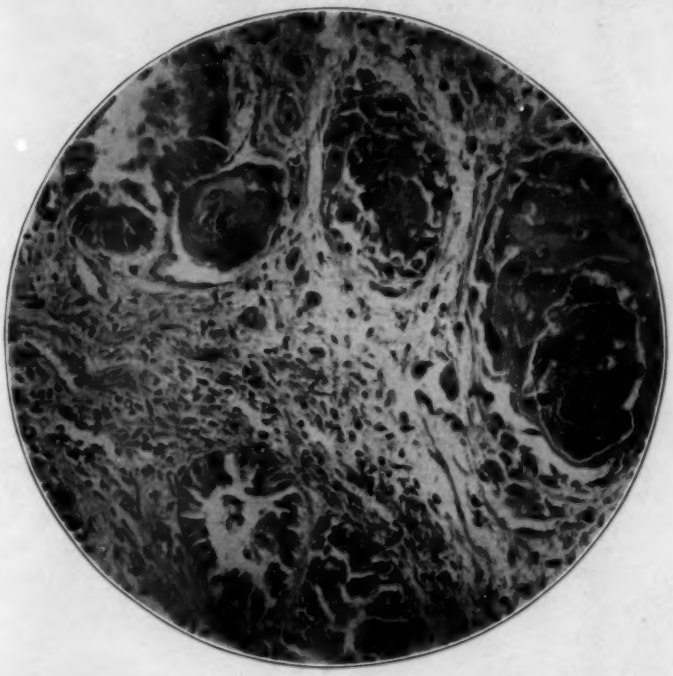

Fig. 3.—Wall of the common bile duct, showing mixed glandular and epidermoid differentiation (× 250).

a portion of the common bile duct. Mixed glandular and epidermoid carcinomatous tissue was present in all coats of the duodenum, including the deeper portions of the mucous membrane, and in the wall of the main pancreatic duct, but none was observed in the pancreas or in the wall of the common duct at this level. The nerves and the perivascular lymphatics were also infiltrated in places.

The carcinomatous tissue was studied in numerous sections, some in serial arrangement. A composite description of the neoplasm follows: In some areas the tumor was composed of loosely arranged masses and columns of undifferentiated small cells which stained rather uniformly but varied in shape. Their nuclei were relatively large and of various shapes, and frequently showed mitotic figures, many of which were irregular. Concentrically laminated whorls were present, composed of keratin material, flat horny cells with eleidin granules, large pale

Fig. 4.—Muscular wall of the duodenum, showing small infiltrating neoplastic nodules (× 100).

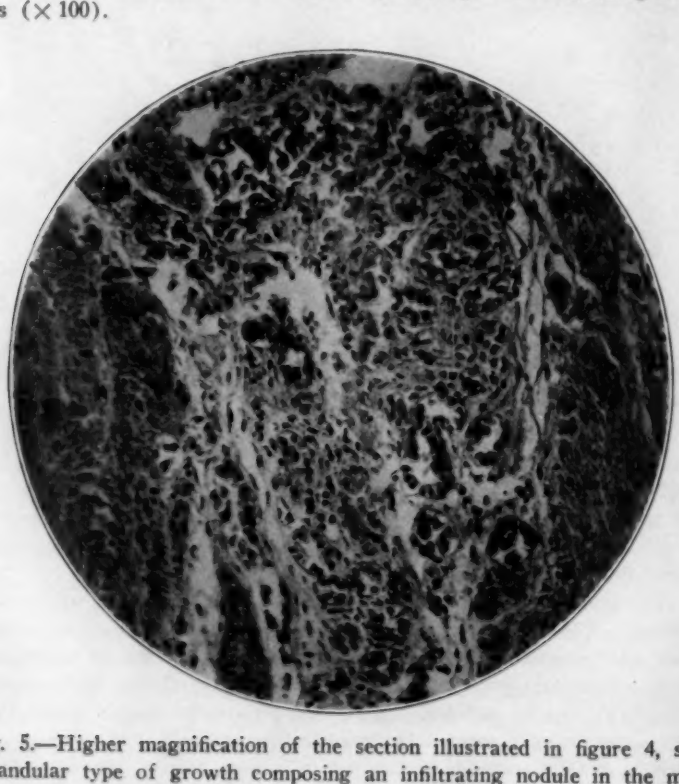

Fig. 5.—Higher magnification of the section illustrated in figure 4, showing the glandular type of growth composing an infiltrating nodule in the muscular wall of the duodenum (× 250).

prickle cells with intercellular bridges and acidophilic inclusion bodies, and deeply stained small basal cells externally. The cells in these epidermoid areas were irregular in size, shape and staining qualities, and many mitotic figures were present, a large proportion of which were irregular and multipolar. In other areas the tumor showed a glandular structure with cuboidal or columnar cells arranged in the form of small or large, round or elongated acini, which occasionally contained degenerated material. These glandular cells were fairly uniform in appearance, with deeply stained granular cytoplasm and large, sometimes multiple nuclei showing frequent mitotic figures. Epidermoid, glandular and undifferentiated cells occurred independently, side by side or intermingled. In one area cells in a transition stage between glandular and squamous cells were observed in some of the large acini. Necrosis and hemorrhage were inconspicuous features. The stroma of the tumor was composed of adult, poorly vascularized connective tissue infiltrated with inflammatory cells.

Associated changes in the liver, gallbladder and kidney were of interest. The liver showed slight degeneration, necrosis and pigmentation of the cells of the inner portion of the lobule and rather marked fibrosis as well as small round cell infiltration of the portal radicles and considerable proliferation of the small bile ducts. The wall of the gallbladder was thickened by hypertrophied muscle and fibrous tissue, and there were many small hemorrhages as well as a few local collections of lymphocytes. The renal epithelium of the convoluted and Henle tubules showed marked degeneration, necrosis and biliary pigmentation. (The significance of these changes in the kidney following biliary obstruction and operative decompression of the biliary tract has been discussed by Lieber and Stewart.[2])

CASES FROM THE LITERATURE

Plenge's Case[3]*—Adenosquamous carcinoma of the peripapillary portion of the duodenum.*

A man aged 54 years died with clinical manifestations suggesting carcinoma of the pancreas with obstruction of the biliary ducts. Autopsy revealed a large, centrally necrotic carcinoma of the duodenum about the papilla of Vater accompanied by infiltration of the head of the pancreas, obstruction of the common and the pancreatic duct and metastasis to the hilar and pancreatic lymph nodes, the liver and both lungs. The neoplastic growth consisted for the most part of strands and cords of flat cells varying in size and shape, and of scattered epithelial giant cells. These cells were frequently connected by intercellular bridges and occasionally formed epithelial pearls. In some areas, especially those adjacent to the normal duodenal mucosa, elongated and round acini lined by a single row of cuboidal and cylindric epithelium were observed. Elsewhere the lining cells were in part cylindric and showed transition to the pavement type. The metastases in the liver, lymph nodes and lungs also showed a mixture of adenocarcinoma and squamous carcinoma.

Lageder's Case.[4]*—Adenosquamous carcinoma of the suprapapillary portion of the duodenum.*

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2. Lieber, M. M., and Stewart, H. L.: Renal Changes Following Biliary Obstruction, Decompression and Operation on the Biliary Tract, Arch. Path. **19**:636 (May) 1935.

3. Plenge, C.: Beitrag zur Frage der Krebse mit ortsfremdem Epithel, Virchows Arch. f. path. Anat. **264**:370, 1927.

4. Lageder, C.: Un caso di carcinoma parapilorico dimorfico del duodeno, con metaplasia epidermoidale e metastasi ovarica, Clin. med. ital. **62**:461, 1931.

A woman aged 49 years, complaining of jaundice, a sense of pressure in the abdomen, loss of appetite and insomnia, died two months after the onset of illness. Autopsy revealed an ulcerated tumor, 5 cm. in diameter, in the posterior wall of the duodenum in its first and second portions. The first portion of the common bile duct was surrounded and obstructed by the neoplastic mass, but the ampulla of Vater was completely free. There were metastases to the liver, regional lymph nodes and right ovary. The tumor varied considerably in the different sections, being almost entirely scirrhous in some and cellular in others, and was accompanied by the formation of acini which occasionally showed papillary projections. In one section there were pronounced pleomorphism and hyperchromasia and numerous mitotic figures. Another section showed a transformation into epidermoid elements, with voluminous cells occurring singly and in groups of ten to twenty or more to form large plaques in the centers of which were fusion of cytoplasm and beginning keratinization.

Mateer and Hartman's Case.[5]*—Adenosquamous carcinoma of the peripapillary portion of the duodenum.*

The patient was a man aged 54 years, with malaise, anorexia, low grade fever, jaundice, epigastric fulness and pain of seven months' duration. At laparotomy there was marked distention of the extrahepatic biliary passages, and a firm mass was palpated adjacent to the head of the pancreas. A cholecystostomy was performed, and the patient died two months later. At autopsy the ampulla of Vater was filled with a friable, grayish tumor mass which extended through the papilla onto the duodenal surface as a flat, rough, granular, nonulcerated nodule, 2 cm. in diameter. There were extension to the head of the pancreas and metastases to the liver and the regional lymph nodes. Microscopic section of the tumor showed unusually large, irregular neoplastic glands lined by high columnar cells intermingled with solid masses of squamous epithelium well differentiated in places but with no distinct epithelial pearls.

Cohen and Colp's Case.[6]*—Squamous carcinoma of the peripapillary portion of the duodenum.*

A woman aged 47 years complained of progressively increasing jaundice, loss of weight, clay-colored stools and dark urine of two months' duration. At laparotomy the common bile duct was opened, and a probe was easily passed into the duodenum. The patient died eight hours after cholecystostomy. At autopsy the papilla of Vater appeared prominent and nipple shaped, and considerable force was required to pass a probe through its orifice, which was surrounded by a small firm mass of whitish tissue. There was an enlarged hard lymph node adjacent to the cystic duct. Histologic sections of the papilla of Vater showed instances of transition from spheroidal cells to typical squamous carcinoma.

Schüssler's Case.[7]*—Squamous carcinoma of the suprapapillary portion of the duodenum* (reported in tabular form only).

A man aged 75 years complained of colic lasting for four months and jaundice for four weeks. Autopsy revealed a stenosing carcinoma of hazelnut size

5. Mateer, J. G., and Hartman, F. W.: Primary Carcinoma of the Duodenum: Clinical and Pathologic Aspects, with Differential Diagnosis, J. A. M. A. **99**: 1853 (Nov. 26) 1932.

6. Cohen, I., and Colp, R.: Cancer of the Peri-Ampullary Region of the Duodenum, Surg., Gynec. & Obst. **45**:332, 1927.

7. Schüssler: Ueber das Verhalten der Gallenblase bei Choledochusverschlussen, Beitr. z. klin. Chir. **115**:433, 1919.

immediately above the papilla of Vater, with extensive metastases in the liver and the lymph nodes. Slightly cornifying squamous carcinoma was the histologic diagnosis.

COMMENT

The incidence of the type of tumor dealt with in this communication is low. Of 416 cases of carcinoma of the peripapillary portion of the duodenum,[8] in 222 the diagnosis was proved histologically; in these, 2 growths were of the squamous, and 2 of the adenosquamous, type, giving an incidence of about 1.0 per cent for each, or a total of about 2 per cent. Of 113 reported cases of carcinoma of the suprapapillary segment (Stewart and Lieber[9]), in 41 there were adequate clinical histories and gross and microscopic studies; of these 41 cases 1 each was of a squamous and an adenosquamous carcinoma, giving an incidence of 2.4 per cent for each.

In the present series, death occurred within two to seven months from the onset of symptoms, the average duration of illness in 5 cases being only four months. Three patients who were subjected to palliative cholecystostomy died eight hours, one day and sixty days, respectively, after operation. There were 4 men and 2 women, with ages ranging from 47 to 75 years, the average age being 54.6 years. All the patients exhibited jaundice, and 3 had abdominal pain. One or more of the following symptoms were also present: a sense of pressure in the abdomen, abdominal distention, loss of appetite, loss of weight, fever and eructations. The liver and occasionally the gallbladder were palpably enlarged and usually tender. However, a correct clinical diagnosis of the cause of the biliary obstruction was not made in any case. At autopsy, metastases were demonstrated in all 6 cases in the regional lymph nodes, in 4 cases in the liver and in 1 case each in the pancreas, lung and ovary.

The origin of the tumors situated in the suprapapillary segment of the duodenum was clearly from the duodenal mucous membrane, but the exact source of the vaterian cancers was obscure. As the source of the latter, five possibilities exist, namely: (1) the duodenal mucosa covering the papilla of Vater, (2) Brunner's glands, (3) the cells lining the terminal end of the common bile duct, (4) those lining the corresponding portion of the pancreatic duct and (5) those lining the ampulla of Vater, when that is present. Because of the complex arrangement, the normal anatomic variation and the intimate relationship of the structures in this small area, together with the tendency for early neoplastic

8. Lieber, M. M.; Stewart, H. L., and Lund, H.: Carcinoma of the Peripapillary Portion of the Duodenum, Ann. Surg. **109**:219 and 383, 1939.

9. Stewart, H. L., and Lieber, M. M.: Carcinoma of the Suprapapillary Portion of the Duodenum, Arch. Surg. **35**:99 (July) 1937.

spread, it is practically impossible to determine the exact point of origin of tumors in the region of the papilla of Vater.

The genesis of squamous or adenosquamous cell carcinoma in this region is unknown. The theory that such tumors may be the result of overgrowth from, or inclusion of, adjoining epithelium of a different type is unsatisfactory, since the distance from the esophagus, the nearest structure normally lined by squamous epithelium, is too great to admit of this possibility. Such neoplasms have also been ascribed to ectodermal rests or inclusions of indifferent cell masses exhibiting postembryonic growth. Metaplasia offers a more obvious and rational explanation, since it may occur in chronically inflamed tissues, especially when they are subjected to chemical or mechanical irritation, such as that inflicted by stones in the biliary ducts. In the series of cases under consideration there is lack of information bearing on this point, although it was stated that cholecystitis was present in 3 cases and gallstones in 1. Several hypotheses have been suggested in explanation of the occurrence of glandular and pavement epithelium in the same neoplasm. The tumor may arise in previously normal glandular epithelium which reverts to a more primitive stage of differentiation (anaplastic metaplasia). Other possibilities include: (1) heterotopia of squamous cells followed by partial differentiation to a higher stage (progressive metaplasia or prosoplasia) and (2) a multicentric origin from heterotopic squamous cells and the adjacent, previously normal glandular epithelium.

SUMMARY

A case of adenosquamous carcinoma of the peripapillary portion of the duodenum is reported. Five additional examples of heterologous metaplasia in this region are reviewed.

GASTRIC CRISIS OF TABES DORSALIS

TREATMENT BY ANTERIOR CHORDOTOMY IN EIGHT CASES

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AND
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Surgical treatment of the gastric crises of tabes dorsalis has only recently offered promising and definite results. It is now recognized that the usual types of antisyphilitic therapy have little effect on such crises. Stokes [1] stated that "marked amelioration of symptoms is possible in 24 per cent, the usual response consisting in reduction in severity and length of attack with or without an increase of intervals between them.—Fever therapy and especially malaria often afford striking temporary relief and the response may even be prolonged."

In outlining intelligently any form of surgical therapy, one must take into account the physiology and the pathologic physiology involved. At present, concepts concerning the physiologic mechanism of visceral pain are controversial, so that in a measure surgical efforts have been of the trial and error type. Indeed, it is more likely that the results of carefully controlled clinical experiences will solve certain physiologic problems than that animal experimentation will do so. For example, it is by no means settled how or by what pathways visceral pain is mediated to the central nervous system. There is a difference of opinion concerning whether a pathologic viscus sends pain impulses to the central nervous system by way of visceral afferent nerve fibers, whether the whole mechanism is one of referred pain, with the pain impulses traversing strictly the somatic afferent fibers, or whether a combination of direct and referred pain obtains.

The theories concerning visceral pain have been adequately reviewed by White [2] and by van Bogaert and Verbrugge.[3] These authors have presented excellent bibliographies.

From the Department of Surgery, Neurosurgical Service, College of Medicine, University of Iowa.

1. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1934, p. 1203.

2. White, J. C.: The Autonomic Nervous System: Anatomy, Physiology, and Surgical Treatment, New York, The Macmillan Company, 1935.

3. van Bogaert, L., and Verbrugge, J.: The Pathogenesis and the Surgical Treatment of Gastric Crisis of Tabes: Neuroramisectomy, Surg., Gynec. & Obst. **47**:543-553, 1928.

However, it is generally agreed that in the case of gastric crises or of any of the forms of pain associated with tabes the lesion involves the roots of corresponding nerves. This simplifies the surgical problem to some extent. Nevertheless, it is still unknown whether such a lesion (with respect to pain) involves visceral or somatic afferent nerve fibers or both and, in the case of visceral afferent fibers, what the remote implications with regard to the visceral nervous system may be.

In this connection it is interesting to note that the "posterior column losses" were minimal in our patients. It would appear that when locomotor ataxia supervenes, indicating an advanced deafferentation, the lesion itself will have destroyed the pain-bearing fibers.

Because of the vagal phenomena (nausea and vomiting) often associated with gastric crisis, it has been felt that the lesion involves the roots of the vagus nerve (Foerster [4]) or that the vagus nerve plays some primary or independent role (Oldberg [5]). Oldberg, in reference to chordotomy, stated: "There are certain things one must not expect this operation to do—one is to relieve the vomiting which is so often associated with gastric crisis of tabes dorsalis. This vomiting is vagal in character and so, of course, would not be affected by a spinal cord operation." This expresses, undoubtedly, a rather general feeling, but the chordotomies in our cases eliminated both pain and vomiting.

Van Bogaert and Verbrugge [3] stated that as far as vagal crises are concerned subdiaphragmatic vagotomy is ineffective and section of the roots of the vagus nerve as proposed by Foerster [4] has not been done sufficiently often to permit one to pass judgment on its merits. In 1 of their cases of the vagal type of crisis, amelioration obtained by section of the thoracic roots was so remarkable that for the time being they have decided to discard the various operations on the vagus nerve.

In addition to insisting on differentiation between splanchnic and vagal crises, Foerster [4] has suggested the importance of the phrenic nerve in certain cases. He concluded that disease of the phrenic nerve causes a special type of crisis, characterized by pain in the shoulder, hyperalgia of the neck and hiccup. Foerster would utilize the radiculospinal operation for the splanchnic form of crisis and section of the roots of the vagus nerve for the vagal forms.

We feel that the outstanding vagal reactions have been misleading. In all probability the nausea and vomiting associated with gastric crisis are a secondary phenomenon and reflex to the primary stimulus. If impulses from the primary stimulus are eliminated, the vomiting should

4. Foerster, D.: Foerster'sche Operation (No. 7): Discussion über den Vortrage des Herrn Kuettner, Verhandl. d. deutsch. Gesellsch. f. Chir., 1910, pt. 1, pp. 29-31 and 42-46.

5. Oldberg, E.: Chordotomy for Relief of Pain, S. Clin. North America **12**:1315-1322, 1932.

cease also. It is unnecessary to assume that the vagus nerve is primarily involved by the lesion in order to explain the associated reactions. Severe stimuli to the vestibular end organ cause nystagmus, dizziness, past pointing and vomiting, but one would not ascribe the nystagmus to a lesion or a direct stimulus of the third, fourth and sixth nerves or the vomiting to a direct stimulus of the vagus nerve. These reactions are integrated responses to the vestibular stimulus, and all are eliminated by section of the vestibular nerve. We feel that the vomiting associated with gastric crisis is in the same sense a reflex response to a severe stimulus of splanchnic afferent nerve fibers, the stimulus occurring at the spinal roots. The mechanism is subserved by the vagus nerve, but if impulses from the primary stimulus were eliminated, this particular reflex mechanism of vomiting would also be eliminated. This procedure would not stop vomiting that is reflex to other stimuli. Frazier [6] has touched on this problem, with much the same conclusions.

Foerster called attention to the important role of the posterior roots in the mechanism of gastric crisis, but posterior radicotomy of even a large number of roots has not been uniformly successful. In opposition to the Bell-Magendie law, he defended the concept that anterior roots conduct certain types of sensibility and stated that in 1911 he began to resect the anterior roots. However, after cutting posterior and anterior roots and even the spinothalamic tracts, Foerster concluded that the pain must take some other route than that which he eliminated. He stated: "One must think of the possibility of pain stimuli being conducted from the stomach by way of the periarterial sympathetic plexus of the gastric vessels, the aortic plexus, the sympathetic trunk, and from there to the cord by the corresponding rami communicantes (eighth cervical to third lumbar roots)."

We feel that herein lies the crux of the problem; that the rhizotomy (of posterior roots) has not been carried high enough.[7] Certainly chordotomies below the third dorsal segment have not been uniformly successful, but in our 8 cases bilateral chordotomy above the third dorsal segment has resulted in complete cure, and there has as yet been no return of pain in any of the cases. Thus, it may well be that some splanchnic afferent fibers course upward in the sympathetic chain to enter the cord at least as high as the third dorsal segment, and if rhizotomy were carried to that level it might be uniformly effective. For this operation to be complete, however, it would be necessary to

6. Frazier, C. H.: Surgery of the Spine and Spinal Cord, New York, D. Appleton and Company, 1918, p. 702.

7. Frazier,[6] in explaining the failures of rhizotomy, suggested the possibility that some afferent sympathetic fibers from the stomach may enter the cord at a level higher than the fifth thoracic segment.

cut the roots from the third dorsal to the twelfth dorsal inclusive and possibly to the second lumbar.

The method of neuroramisection (technic of von Gaza) has been used by van Bogaert and Verbrugge.[3] It consists of extraspinal section of about the sixth to the tenth spinal nerve, including section of the rami communicantes to these nerves. If the lesion is in the posterior roots, it is difficult to see how this operation can be effective. All visceral and somatic afferent fibers are severed distal to their cell bodies as well as distal to the lesion. Three cases are reported. In the first case, the seventh to tenth dorsal nerves with their rami were severed on the right. The patient seemed better and was relieved of pain, but died in three weeks of cachexia. In the second case, the seventh to eleventh dorsal nerves and their rami were severed on the right. After three months the crises returned. The fifth and sixth nerves on the right were severed, resulting in cure for more than a year. In the third case, the sixth to tenth dorsal nerves and their rami were severed on the left. Six months after operation the pain remained suppressed on the left, but not entirely on the right, and the mild gastric disturbances were not improved.

Frazier [6] summed up the situation to 1918 by listing the operations which are directed at peripheral nerves and those which result in degeneration of posterior roots. Among the former he discussed stretching of the solar plexus (Jaboulay, 1900). (The technic of von Gaza should be included here.) Among the latter he discussed the following methods: 1. Extraction of the peripheral nerves with their ganglions. This operation has been associated with a high morbidity and mortality, and its effectiveness depends on destruction of the posterior roots. 2. Extradural ganglionectomy (Sicard and Desmorest, 1912). This should be applicable only to lesions of the thoracic region. At the time of Frazier's report the operation had not been given sufficient trial. 3. Extradural rhizotomy (Guleke, 1910). This does not differ in effect from intradural section of posterior roots except that it unnecessarily includes anterior roots. 4. Ligation of both anterior and posterior roots (Sauve and Tinel, 1913). 5. Intradural rhizotomy (Foerster, 1909). This has been discussed previously. It was endorsed by Frazier as the most logical procedure. Frazier stated that the sensory sympathetic supply of the gastrointestinal tract includes positively the fifth to twelfth thoracic nerves and possibly the first and second lumbar nerves. Although in most cases crises originate between the level of the seventh and that of the ninth thoracic segment, many patients are not relieved by section restricted to this region. The results of Foerster's rhizotomy, based on 73 cases in the literature, are expressed as follows: 2 in 10 patients cured; 4 in 10 improved; 1 in 10 unimproved, 1 in 10 dead and the remainder not clearly reported on or dead soon thereafter.

Frazier did not condemn chordotomy, but by 1918 there had not been sufficient experience with this procedure to warrant conclusions. Kahn and Barney [8] reported the case of a patient in whom a bilateral chordotomy was done at the level of the fifth thoracic segment. The level of loss of pain was at the umbilicus, and the crises were not relieved. The splanchnic nerves were sectioned, and later the rami communicantes of the eleventh and twelfth thoracic nerves. The pain still being unrelieved, a bilateral chordotomy was done at the seventh cervical segment and was followed by complete relief.

Mixter and White [9] reported the case of a patient who had severe pains in the left lower ribs and in the left side of the abdomen for four years. He was addicted to the use of morphine and had had three previous operations. Bilateral chordotomy failed, but the operation was not complete, as was shown by sensory examination. Section of the posterior roots from the fifth to the tenth dorsal inclusive gave no relief. Removal of the seventh to the ninth sympathetic ganglion gave relief from the pains in the left side of the abdomen. Lastly, ramisectomy from the fourth to the seventh dorsal segment inclusive gave relief from the thoracic pain.

White [2] (page 288) reported the case of a patient in whom portions of the right major and minor splanchnic nerves were resected beneath the diaphragm. The patient was relieved of severe pain in the right upper quadrant of the abdomen for two months, but the pains shifted to the right lower quadrant. It was necessary to perform a chordotomy to obtain complete relief. White stated that in the future he intended to utilize von Gaza's ramisectomy or injection of alcohol and procaine hydrochloride into the thoracic rami as the therapy of choice for gastric crises. He had concluded that section of the spinothalamic tract should be reserved for patients who fail to obtain relief with other operations or for patients with widespread involvement of the lower extremities.

Platou and Säthre [10] reported a case of gastric crisis in which complete cure to the time of writing (twelve months) was obtained after bilateral chordotomy at about the second and third dorsal segments.

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8. Kahn, E. A., and Barney, B. F.: Anterolateral Chordotomy for Intractable Pain of Tabes Dorsalis, Arch. Neurol. & Psychiat. **38**:467-472 (Sept.) 1937.

9. Mixter, W. J., and White, J. C.: Pain Pathways in the Sympathetic Nervous System: Clinical Evidence, Arch. Neurol. & Psychiat. **25**:986-997 (May) 1931.

10. Platou, E., and Säthre, H.: Chordotomie (Durchtrennung der Schmerzbahnen im Rückenmark) bei Tabes dorsalis, Acta chir. Scandinav. **75**:258-272, 1934.

So far as we can ascertain, Benedek and Hüttl [11] are the only authors who have expressed definitely the belief that chordotomy is an ineffective and dangerous treatment for gastric crises. After an experience with 3 cases they endorsed conservative therapy and stated that they would turn to chordotomy only as a last resort. In their first case the crises returned after a month. The patient in the second died after the operation, and the patient in the third acquired pains in the legs after the operation.

We would, of course, advise that conservative therapy be given a trial and certainly that the syphilis be given adequate treatment before an operation is considered. However, it should be borne in mind that such drastic therapy as the malaria treatment will often have a severe influence on a patient who already is in a poor state of health. This treatment gave practically no benefit in our cases, and in certain instances it had to be terminated because of untoward reactions. Conservative therapy can at times be more radical than certain forms of operative therapy.

We are reporting 8 cases of gastric crisis treated by anterior chordotomy. The first case is reported somewhat in detail in order to demonstrate the motor and sensory effects of complete section of the anterior quadrants of the cord. Cases 2 and 3 have been reported in a previous communication.[12]

REPORT OF CASES

CASE 1.—J. J., a white man aged 38, was referred to the department of neurology on June 16, 1937, by Dr. Robert Netolicky, of Cedar Rapids, Iowa.

Since 1935 he had suffered severe spells of vomiting accompanied by acute abdominal pain. At first these attacks occurred every six months. They had progressed in frequency since January 1937, there being at least one attack every month. Not only the attacks but the fear of them had broken the patient's morale and had caused a loss of 35 pounds (16 Kg.) in weight in the past ten months.

In 1935 it was found that he had a positive Wassermann reaction. Antisyphilitic therapy, consisting of forty intravenous and thirty intramuscular injections, was given. The patient had no knowledge of a primary lesion.

Past History.—He had been in good health until 1935. Appendectomy and an operation on the gallbladder were performed in that year.

Examination.—The patient was dejected and badly nourished. Although Argyll Robertson pupils were present, the neurologic examination otherwise gave essentially negative results. There was no clinically demonstrable involvement of the posterior columns.

Laboratory Data.—The value for hemoglobin was 14 Gm. per hundred cubic centimeters of blood. There were 5,300,000 erythrocytes and 5,700 leukocytes per

11. Benedek, L., and Hüttl, T.: Ueber den Wert der Chordotomie bei "Crise gastrique," Beitr. z. klin. Chir. **161**:621-644, 1935.

12. Hyndman, O. R., and Van Epps, C.: Possibility of Differential Section of the Spinothalamic Tract: A Clinical and Histologic Study, Arch. Surg. **38**:1036-1053 (June) 1939.

cubic millimeter of blood. The smear was normal. The urine was normal. The Wassermann reaction of the blood was 4 plus.

The pressure of the spinal fluid was 110 mm. of water with the patient in the prone position. There were 200 lymphocytes per cubic millimeter. The reaction for globulin was 3 plus, the gold curve 1122200000 and the Wassermann reaction 3 plus.

Treatment and Course.—The patient was inoculated with malarial blood. Eight days later he had the first chill. He was permitted to have only six chills, because his condition became poor. The attacks of abdominal pain became frequent, necessitating numerous hypodermic injections of morphine. These, as well as administration of chloral hydrate, sodium bromide and sodium amytal (intravenously, 15 grains [0.97 Gm.] daily) gave only fair relief.

Section of the spinothalamic tracts was advised, and the patient was transferred to the surgical service. During the succeeding five days he had daily attacks of severe gastric crises. These consisted of repeated vomiting, hard retching, excruciating pain and profuse sweating. He stated that it felt as though his abdomen were being squeezed in a vise. He was able to take and retain very little nourishment. He appeared pale and exhausted, and the level of hemoglobin had fallen to 12 Gm. He became so despondent that he attempted to strangle himself with a cord tied to the side of the bed.

Examination.—An attempt was made to obtain as definite a clinical impression as possible of the sensory and motor status and the muscular tone. The following findings represent the consensus of three examiners.

Motor Status: The strength of the extensor and flexor muscles of the legs and ankles was normal. The calf muscles were normal to palpation. The heel to knee and the toe to finger test were well performed. Alternate movements of the legs were well performed. Station was maintained well with the eyes closed and the heels together. The patient hopped well on one foot, walked a straight line well and turned without faltering. The reflexes were as follows:

	Biceps	Knee Jerk	Achilles Tendon	Plantar	Abdominal
Right	2+	2+	1+	Flexion	0
Left	2+	2+	1+	Flexion	0

Sensory Status: The following data were obtained:

	Shins	Hands
Pain	100 per cent	100 per cent
Cotton	100 per cent	100 per cent
Heat	100 per cent	100 per cent
Pallesthesia	100 per cent	100 per cent
Two point discrimination	8 cm.	5 cm.
Sense of position	Good	Good

The soles were normally ticklish.

There was an area of hyperesthesia corresponding to the segments from the ninth dorsal to the first lumbar.

Operation.—The second, third and fourth dorsal laminal arches were removed. The third posterior root on each side was sectioned. In order to assure complete abolition of pain, a cataract knife was inserted deeply, as shown in figure 1, and the point was brought out at the anteromedian fissure. The same procedure was carried out on the opposite side at a slightly different level. Some bleeding was encountered but was easily controlled with cotton pledgets and warm saline solution.

The operator (O. H.) is convinced that he sectioned the entire anterior half of the cord and consequently all of the descending extrapyramidal tracts except possibly the posteriorly placed rubrospinal tracts.

Course.—The patient made an uneventful recovery. All the symptoms related to the gastric crises, including pain and vomiting, have been completely abolished to the time of writing (twenty-five months).

Discrimination of pain and temperature was abolished from the fifth dorsal segment down, although sensitivity to light touch, pressure and vibration, two point discrimination and sense of position were not essentially impaired at any time.

For about ten days the patient complained of "girdle pain" in the third dorsal segment, but the pain (as well as a degree of hyperesthesia) was limited to this segment.

For five days (including the day of operation) he was unable to move his legs. On the sixth day voluntary function began to return and progressed gradually to 100 per cent recovery. During the five day period the paraplegia was flaccid, with complete absence of all reflexes, including the flexion reflexes. On the seventh day the knee jerks were 1+ bilaterally, and they developed gradually to 2+ by

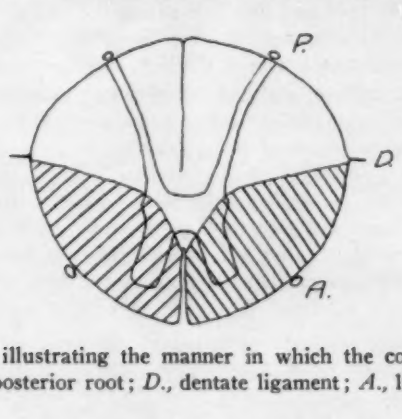

Fig. 1.—Diagram illustrating the manner in which the cord was sectioned in case 1. *P.* indicates posterior root; *D.*, dentate ligament; *A.*, line of anterior roots.

the twenty-fourth day. The achilles tendon jerks made their feeble appearance several days after the appearance of the knee jerks and developed to 1+ bilaterally by the twenty-fourth day. Response to plantar stimulation appeared after the return of the ankle jerks and was present to a normal degree by the twenty-fourth day.

Since the operation there has never been the slightest semblance of so-called upper motor neuron signs—extensor spasticity, hyperactive deep reflexes, dorsiflexion of the great toe, or ankle or patellar clonus.

Voluntary control of the bowels and bladder was lost for about sixteen days and then gradually returned to normal.

The patient felt most grateful for the relief from his crises. His interest in life and his ambition returned, and when he realized that he could retain food his appetite increased rapidly.

One month after the operation the flexor and extensor strength of his legs was 100 per cent. During recovery there was never the slightest evidence of asynergy, ataxia, incoordination or tremor. The heel to knee and the toe to finger test were normally performed. In short, when motor movement became possible, there was never any disturbance in the pattern.

Caloric tests were done prior to operation, and, although nystagmus and past pointing of the upper extremities were normal, for some reason there was no past pointing of the lower extremities, and consequently this study failed to attain its intended significance postoperatively.

It was obvious on palpation that the muscles of the thighs and calves were soft, flabby and without tone. At the time the patient was discharged (the twenty-ninth postoperative day) he was walking and performing in all respects with normal movement pattern but was easily fatigued. A walk of twenty steps would cause him to perspire from fatigue. Motion pictures were taken as a record of his gait.

Follow-up Examination.—Six months after the operation a follow-up examination revealed the patient to be healthy appearing, contented, ambitious and grateful, with no complaints. He had been working full time at his trade, carpentry and mechanics. He worked on and around scaffolding with ease. He had gained 25 pounds (11.5 Kg.) since his operation. He slept well. He had full control of the bowels and bladder.

Motor Status: The neurologists who examined the patient, Dr. Clarence Van Epps and Dr. C. G. Barer, stated that they were unable to elicit a single motor abnormality of the lower extremities. Station, gait, hopping and running were normal and were accompanied by no more than ordinary fatigue. Alternate movements of the lower extremities were normal. There was no evidence of asynergy, ataxia or incoordination. The reflexes were as follows:

	Biceps	Knee Jerks	Achilles Tendon	Plantar
Right	2+	2+	1+	Flexion
Left	2+	2+	1+	Flexion

The thigh and calf muscles were normally firm and solid to palpation, and the patient could hold his leg suspended from the table exceptionally well without becoming fatigued.

Sensory Status: There was loss of appreciation of pain and temperature from the fifth dorsal segment down.

The cutaneous reactions of the shins to various tests and stimuli were as follows:

Pain	0
Cotton	100 per cent
Heat	0
Pallesthesia	100 per cent
Two point discrimination	8 cm.
Sense of position	Good

At present the lower extremities feel comfortable and are never numb. There is a mild sensation of warmth. The patient can sense accurately when the hairs of his legs are pulled, but the sensation is unaccompanied by pain. He states that a pin scratch feels like the dragging of a blunt stick across his skin. The soles continue to be as ticklish as they were prior to chordotomy. He senses accurately breath blown on his lower extremities but cannot discriminate its temperature. He cannot appreciate the presence of water on his legs, and once he was unaware that his trousers were soaking wet. The psychic power of erection is completely lost, and, though a moderate desire for intercourse remains, the act is impossible. On occasions, however, in the morning before the bladder is emptied, he has noticed an erection.

He has remained well to the time of writing (two years).

Case 2.—L. K., a white man aged 56, was referred by Dr. Charles Dimond, of Keokuk, Iowa, on June 8, 1937.

He complained of severe attacks of abdominal pain and vomiting for the past three years, loss of 15 pounds (7 Kg.) in weight in the past six months and difficulty in voiding urine for ten years. The abdominal crises consisted of sharp attacks of colicky pain referred to the epigastrium. The attacks were accompanied by vomiting and retching but were unassociated with meals. They often occurred on several successive days. They occurred at least once a week and were relieved only by hypodermic injections of morphine.

He contracted syphilis in 1913 and stated that he had had one hundred injections, intravenous and intramuscular, since that time.

Examination.—The positive findings on neurologic examination were: absence of the pupillary reaction to light and in accommodation; weak knee jerks on reenforcement; absence of the right ankle jerk on reenforcement, and slight swaying with the heels together and the eyes closed.

Laboratory Data.—The blood and urine were normal. The spinal fluid contained 16 lymphocytes per cubic millimeter and 40 mg. of protein per hundred cubic centimeters. The Wassermann and Kahn reactions were positive on one occasion and negative on two.

Treatment.—The patient was given malaria therapy, but the blood pressure dropped so low with the fifth chill that the treatment was terminated. He then received courses of neoarsphenamine, a bismuth compound and tryparsamide. During the treatment he had a gastric crisis lasting six days.

He was discharged in August with instructions to continue treatment and progressed satisfactorily until December, when the crises returned with their previous severity. From this time on he had a continuous girdle-like sensation about the waist and continued to lose weight.

He returned to the hospital on March 20, 1938.

Operation.—On March 26 the second, third and fourth dorsal arches were removed, and a bilateral chordotomy was performed in the region of the third segment. The right spinothalamic tract was completely sectioned; on the left a superficial anterior section was made so as to eliminate pain in the chest and abdomen without involving that in the leg.[13]

Function of the bladder was regained on the day after the operation, and motor function of the lower extremities was not impaired.

Result.—The patient has been free of both pain and vomiting to the time of writing (sixteen months).[14]

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13. Differential section of the spinothalamic tract has been discussed in a previous paper,[12] in which the case of this patient was reported, with diagrams illustrating the pattern of the section and the sensory changes.

14. At the time the proof of this paper was read the patient had returned to the hospital complaining of a recurrence of the crises. On Nov. 13, 1939, the analgesia over the right side of the chest was found to have practically disappeared. Anterior chordotomy was repeated, the section being made between the fifth and the sixth cervical segment on the left and between the sixth and the seventh cervical segment on the right. Sensibility to pain and temperature was lost to the level of the third dorsal segment bilaterally. The patient recovered uneventfully, and crises have been abolished to the time of writing (two months).

This case teaches that unilateral chordotomy will not abolish gastric crises. While differential chordotomy is a possibility, it is not wise to attempt less than a complete section of the spinothalamic tracts in the treatment of gastric crises.

CASE 3.—C. K., a white man aged 27, was referred in April 1938 by Dr. C. M. Wray, of Iowa Falls, Iowa.

Three years previously his illness had begun with attacks of nausea and vomiting associated with very little pain. They occurred at least once a month. After a year, sharp, nonradiating epigastric pain was associated with the attacks, and the frequency increased so that he had an attack at least each week. As a rule the attacks lasted several days; occasionally they lasted as long as ten days. In contradistinction to most of the other cases in this series, the nausea and vomiting appeared to be more severe than the pain.

In June 1937 a gastroenterostomy had been performed, after a diagnosis of peptic ulcer. The Wassermann reaction was later found to be 4 plus, and he was given sixty-four intravenous and sixty-four intramuscular injections.

In the past few months he had wet the bed on several occasions.

He had lost weight steadily during the past three years.

During his stay in the hospital before operation (one month) he seldom had a two day period free of pain and vomiting. During the attacks, which would last usually a day and a night or two days, it was necessary to stop administration of anything by mouth and to give chloral hydrate by rectum and fluid by vein.

Examination.—It was striking that the usual signs of tabes were minimal. The pupils were normal. The deep reflexes were absent. Sensation was well preserved except for some diminution of two point discrimination and sense of position in the lower extremities. There was slight swaying with the heels together and the eyes closed.

The Wassermann reaction of the spinal fluid was 4 plus.

Roentgen examination after administration of a barium sulfate meal revealed a functioning gastroenterostomy opening and an otherwise normal stomach.

Operation.—On May 5 the first, second and third dorsal laminal arches were removed and bilateral chordotomy was carried out with the region under local anesthesia. (This case was reported in a previous paper,[12] in which are given diagrams to illustrate the manner in which the cord was sectioned and the results of sensory examination.) On the right a complete section of the anterior quadrant was made from the dentate ligament to the anterior median fissure. On the left the section was begun at a point halfway between the dentate ligament and the anterior root and carried to the anterior median fissure.

Result.—Recovery was uneventful except for retention of urine requiring catheterization for two weeks. The patient voided occasionally during this period but retained some residual urine. He was voiding well when discharged, three weeks after the operation.

Pain and temperature sensibility were lost to the nipple line, but there were no demonstrable changes in other forms of sensation by routine tests. Motor function in the lower extremities was weak for several days but rapidly returned to normal before the patient's discharge.

There was no semblance of an attack while the patient was in the hospital.

A check-up examination four months later revealed no subsequent changes in the sensorium. The patient's strength was normal, and he had gained 20 pounds (9 Kg.). He had no difficulty in voiding urine. Since leaving the hospital he had had four brief attacks of vomiting without pain. He was happy over the result and has remained well to the time of writing (fifteen months).

CASE 4.—R. R., a white man aged 28, was referred by Dr. A. J. Meythaler, of Earlville, Iowa, on Sept. 16, 1938.

He complained of severe abdominal pain and vomiting of one month's duration. On August 28 he was suddenly seized with a severe, knifelike epigastric pain which radiated to the umbilicus, and he immediately began to vomit. The pain had continued almost without interruption until his admission, except for periods of relief from hypodermic injections of morphine sulfate (four to six daily). Vomiting was extreme. There were periods of intractable hiccup. He had no desire for food, and the sight or smell of it brought on severe nausea and retching. During several days prior to his admission the pain and vomiting had gradually lessened, and these symptoms were slight when he reached the hospital. After five days in the hospital they subsided completely, and he left, spurning treatment, against the advice of the staff. Six days later the pain and vomiting suddenly began again and grew steadily worse. He reentered the hospital on October 5, anxious to accept any therapy for relief.

In 1930 the patient had had a penile lesion. In February the Wassermann reaction had been 4 plus and he had been treated by intravenous and intramuscular injections until September. There had been no other manifestation of tabes. He had suffered from perennial asthma for years.

Examination.—When first seen the patient was doubled up, in the knee-chest position, pressing his fists into his abdomen and retching and vomiting constantly. He was acutely ill, with evidence of marked loss of weight. The right pupil was dilated and the left irregular. The pupils reacted in accommodation but not to light. Except for lessened activity of the patellar reflexes there was no evidence of neurosyphilis. Sibilant rales and rhonchi were heard over both lung fields. The abdominal muscles were voluntarily spastic, and there was slight epigastric tenderness. There was a penile scar.

Laboratory Data.—The value for hemoglobin was 90 per cent. There were 4,500,000 erythrocytes and 4,600 leukocytes per cubic millimeter of blood. The Wassermann reaction of the blood was 4 plus. The spinal fluid was clear; it gave a negative reaction for globulin and a negative Meyers reaction. The spinal fluid pressure was normal. The fluid contained no cells. The Wassermann reaction was positive. The concentration of total protein was 50 mg. per hundred cubic centimeters.

Operation.—On October 12 an anterolateral chordotomy was performed at the level of the second and third thoracic segments. Immediately after section of the anterior columns, pain and temperature senses were lost to the axillary level.

For forty-eight hours after the operation there were complete motor paralysis of the lower extremities and complete retention of urine. Motor function slowly returned, and when he left the hospital, on the twenty-fifth postoperative day, he was able to walk and function of the bladder had returned.

From the operation to the present time (nine months) he has not vomited. His pain was immediately and completely relieved and has not recurred. His appetite is good, and he has gained 10 pounds (4.5 Kg.). There is low grade cystitis which causes frequency of urination. He is most happy with the result.

Case 5.—J. L., a white man aged 56, was referred by Dr. John T. Hecker, of Cedar Rapids, Iowa, on Sept. 30, 1938, with complaints of severe abdominal pain, nausea, vomiting and loss of weight for six years.

In July 1932 he was suddenly seized with severe, gripping pain over the entire abdomen, and he vomited in projectile fashion. This occurred almost daily until December 1932, when a stoneless gallbladder was removed. After the operation, while still in the hospital, he had an identical attack; this prompted his first Wassermann test, which elicited a positive reaction. During the subsequent intensive

antisyphilitic treatment he had no further attacks. Identical episodes began again in 1935, recurring at short intervals. For three months prior to his admission he had scarcely been free of pain for a day, had taken daily hypodermic injections of morphine sulfate and had lost 18 pounds (8.2 Kg.). The pain and vomiting became more and more severe.

Gonorrhea was contracted in 1899, but syphilis had not been suspected.

Examination.—The patient was cachectic and pallid. He presented no positive neurologic abnormality other than irregularity of the left pupil, bilaterally poor pupillary reaction to light and reduction of pallesthetic sense over both tibias.

Laboratory Data.—The blood and the urine were normal. The Wassermann reactions of both the blood and the spinal fluid were negative. The result of the Kahn test was equivocal. The spinal fluid contained 15 lymphocytes per cubic millimeter. It gave a negative reaction for globulin. The value for total protein was 37 mg. per hundred cubic centimeters.

Roentgen examination of the stomach and of the duodenal bulb showed no lesion.

Operation.—On October 17 an anterolateral chordotomy was performed at the level of the second and third thoracic segments, with the region under local anesthesia. Pain and temperature senses were immediately lost to the nipple line. There was transient paralysis of both legs for forty-eight hours after the operation, with the usual brief period of retention of urine. There was no further abdominal pain or vomiting. The patient left the hospital on the eleventh postoperative day, ambulant and satisfied with the result.

He gained weight and strength and was planning to return to work, but on November 8 he died suddenly, with cerebral hemorrhage suspected as the cause.

CASE 6.—A. R., a white man aged 49, was referred by Dr. F. N. Cole, of Iowa Falls, Iowa, in February 1939.

He had been treated in this hospital off and on since 1935. His complaints at that time were dribbling of urine, shooting pains in the legs, failing vision and crawling sensations in the hands and feet. He was given routine antisyphilitic treatment and a course of malaria in 1937. He was improved for a time, but the shooting pains in the legs returned, and in December 1938 he had girdle pains associated with nausea and vomiting. On his present admission to the hospital these crises were occurring daily, and food was difficult to take and retain. He had lost 15 pounds (6.8 Kg.) in the past two months.

Examination.—The significant findings were irregular and unequal pupils with a sluggish reaction to light. The deep reflexes were obtained on reenforcement. There was absence of sensation to pain over the shins. The station and gait were normal.

Laboratory Data.—There was mild secondary anemia. The urine was normal. The spinal fluid contained 57 lymphocytes per cubic millimeter. The Wassermann reaction was 3 plus. The pressure was normal.

Operation.—On February 8 the upper three dorsal laminal arches were removed with the region under local anesthesia. The cord appeared smaller than normal, and the arachnoid was somewhat thickened. Bilateral incisions were made into the cord, beginning about 2 mm. anterior to the dentate ligament and emerging about 3 mm. mesial to the anterior roots and being 2.5 to 3 mm. deep. The levels of the incisions were separated by about 2 cm. The patient was tested and found to have lost sensibility to pain to the nipple line.

Course.—Save for a transient infection of the upper respiratory tract the patient made an uneventful recovery. He was discharged in ten days. He was incontinent

to about the same degree as before operation. Eight days later he returned because of cystitis, which responded well to the usual management. He has since remained in good health and completely relieved of the crises (five months).

CASE 7.—A man aged 65, a physician, complained of pain from gastric crises of eight months' duration.

He had contracted syphilis in 1897, but after treatment with mercury compounds and iodides he was free of symptoms until 1912. He then had photophobia and visual difficulties. Changes in the pupils were disclosed, and the Wassermann reaction was positive. After treatment with arsphenamine and later with neoarsphenamine and bismuth preparations the Wassermann reaction of the blood became negative and remained so. He had "lightning pains" in the legs in 1919; these became so severe that he was compelled to quit his practice in 1937. The gastric crises began eight months ago. The attacks consisted of severe epigastric pain without radiation and were always accompanied by nausea and vomiting. There had been as many as eight attacks in twenty-four hours. He had taken morphine sulfate and dilaudid hydrochloride in increasing doses, so that when examined he alternated between ⅓ grain (24 mg.) of the former and 1/16 grain (4 mg.) of the latter every two hours.

Examination.—The positive findings were: unequal, enlarged pupils reacting very slightly to light; absence of knee and ankle jerks; a slightly ataxic gait, and diminished sensation to pinprick over the shins. Ability to void was diminished, and there was about 100 cc. of residual urine.

Laboratory Data.—Routine examinations of the blood and urine gave essentially negative results. The Wassermann reactions of the blood and spinal fluid were negative.

Operation.—On March 28, 1939, the upper three dorsal laminal arches were removed. The second posterior thoracic root was sectioned on each side, and bilateral chordotomy was performed in the same manner as in case 6. Cutaneous sensibility to pain and to temperature was lost to the nipple line.

Course.—The postoperative course from a surgical standpoint was uneventful, but the problem of withdrawal of narcotics had to be met with the greatest patience. The morphine and dilaudid were gradually replaced by codeine over a period of ten days and at the time of his discharge, twenty-five days after the operation, he was receiving only 1 grain (0.06 Gm.) of codeine sulfate every three hours. During the withdrawal of morphine he complained of vague pains in the legs, bladder and rectum. The origin of these pains must undoubtedly have been central. There was the usual postoperative retention of urine. He regained the ability to void urine before leaving the hospital but carried about 300 cc. of residual urine. The gastric crisis syndrome (pain and vomiting) did not reappear. The strict withdrawal of narcotics, however, was poorly tolerated, and he died of circulatory failure two months later, after a ten day period of delirium.

CASE 8.—A. R., a white man aged 33, had had lightning pains in the legs beginning two years prior to examination. Shortly thereafter he began having attacks of pain in the chest. The pain was located in the epigastrium and did not radiate. He had a sense of constriction as if a band were being tightened about the lower part of the chest. Vomiting and retching with the attacks were marked. He stated that he had vomited as many as forty times in one day, and he felt that the vomiting was worse than the pain. The attacks occurred at intervals of about two months and continued for three to four weeks. He had acquired an aversion

to food and during the attacks could not keep even a teaspoonful of water on his stomach. There had been some dribbling of urine and also difficulty in starting the urinary stream.

Examination.—The positive findings were: Argyll Robertson pupils; knee and ankle jerks present only on reenforcement; a positive Romberg sign, and delayed pain sensation over the shins. There was hydronephrosis on the left.

Laboratory Data.—Moderate anemia following malarial treatment was present. There were 3,830,000 red cells per cubic millimeter of blood. The urine was essentially normal except for many red cells at times. The Wassermann reaction of the blood was positive.

Spinal Fluid.—Dynamic and cytologic tests gave negative results. The Wassermann reaction of the spinal fluid was doubtful.

Treatment.—The usual antisyphilitic therapy was given. Malaria was induced, and four severe chills were allowed to occur. It was the impression that the malaria initiated an attack of gastric crisis which persisted for two weeks.

Operation.—On April 25 a bilateral chordotomy was done (with the use of local anesthesia) at the second and third dorsal segments, as in the previous case.

Course.—Cutaneous sensibility to pain and temperature discrimination were lost to the seventh rib on the right and to the nipple on the left. Ability to void returned in nine days, but dribbling continued the same as before operation. His course was uneventful, and he was discharged, walking normally, on the sixteenth day. The gastric crises, including pain and vomiting, have not reappeared to the time of writing (three months).

COMMENT

In our 8 cases the results were gratifying to the patients and to us. These are the only patients for whom we have attempted surgical treatment thus far. We feel that chordotomy guarantees relief from crises, but certain demands must be fulfilled. The chordotomy should be bilateral and should be carried out preferably at the second dorsal segment—not lower than the third. The spinothalamic tracts must be completely sectioned, the cutaneous level of loss of sensibility to pain being brought to the nipple line.

From an experience with sixty chordotomies, one of us (O. H.) feels that he has deduced the fact that spinothalamic tracts are farther anterior in the cord than is ordinarily believed. An incision 3 mm. deep beginning 2 mm. anterior to the dentate ligament and carried 3 mm. mesial to the anterior root will section the tract completely at an upper dorsal level (fig. 2). The 2 mm. region anterior to the dentate ligament is "silent" so far as pain and temperature are concerned. Unless the section is carried beyond the anterior root the level of loss of sensibility to pain will not be at its maximum height and the section will not be complete.

There are disadvantages which must be accepted with bilateral chordotomy: loss of cutaneous sensibility to pain and temperature; retention of urine necessitating catheterization for ten days to two weeks; the possibility of serious consequences from any incision of

the cord (although none occurred in these cases), and the loss of sexual function (erection and orgasm). None of our patients appeared to regret the loss of sexual function. One other patient, however, has refused the operation for this reason.

We feel that the significant advantage of chordotomy in the treatment of intractable gastric crises is that it offers practically certain abolition of the pain and vomiting after one operation, an operation which requires a small laminectomy.

A patient who has spent many hours over a vomiting basin, suffering agonizing and relentless pain, and who has come to dread the sight of food is in a desperate frame of mind. It is striking to note how apprehensive the patients are for a few days after the operation lest ingestion of food bring on an attack. When they are confident that the pain and vomiting have been eliminated, they show complete reha-

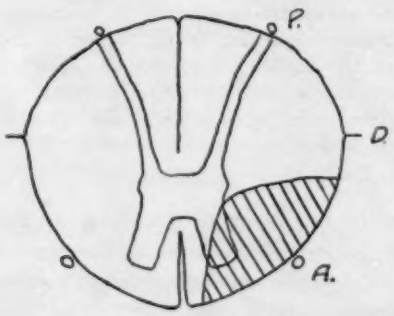

Fig. 2.—Diagram to illustrate the manner in which a section is made to include the entire spinothalamic tract at a high dorsal level. *P.* indicates posterior root; *D.*, dentate ligament; *A.*, line of anterior roots.

bilitation of their mental outlook. Their appetites improve greatly, the hemoglobin content of the blood increases and they gain weight. All the patients in this series have been grateful and anxious to return to a gainful occupation.

SUMMARY

Eight cases of gastric crises of tabes dorsalis are presented. The patients were treated by bilateral chordotomy at the second and third dorsal segments. In case 1 complete section of both anterior quadrants of the cord was made and careful studies of motor function carried out. In case 2 the spinothalamic tract on the right was completely sectioned. That on the left was partially sectioned in order to eliminate pain only in the chest and abdomen on that side. In the remaining cases the spinothalamic tracts were sectioned completely on both sides.

In case 5 the patient was free of pain and vomiting from the time of operation, October 17, until death on November 8, with cerebral

hemorrhage suspected as the cause. In case 7 the patient died from withdrawal of habitually used narcotics two months after the operation. The crises were eliminated during this period, however. The other 6 patients have remained completely free of pain and vomiting to the time of writing (twenty-five, sixteen, fifteen, nine, five and three months respectively), with the exception of the patient in case 3, who has had short periods of vomiting on several occasions without pain. This patient had previously had a gastroenterostomy.

After the operation, function of the bladder was regained in sixteen, one, fourteen, seven, seven, ten, twenty and nine days respectively. All the patients were walking alone when they left the hospital except 1 (case 7), who had not yet attempted to walk because of weakness from withdrawal of narcotics.

CONCLUSIONS

Complete bilateral section of the spinothalamic tracts above the third dorsal segment abolishes the pain and vomiting associated with the gastric crises of tabes.

Retention of urine and occasional motor weakness are transient sequelae. Loss of sexual function is permanent. Considering the beneficial results of this procedure, its disadvantages are minimal.

SEVENTY-FIRST REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

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CONGENITAL DEFORMITIES

Congenital Pseudarthrosis of the Tibia.—Scott [1] briefly discusses the condition known as congenital pseudarthrosis of the tibia and presents a case in which the patient has been carefully followed from birth to the age of 4 years. He classifies patients with this type of deformity as follows: (1) those with well marked anterior angulation, with no fracture at birth; (2) those who show slight deformity at birth but in whom fracture and pseudarthrosis develop after slight trauma; (3) those who have had pseudarthrosis since birth, and (4) those who are normal at birth but in whom fracture and pseudarthrosis develop later. The author's patient, at birth presented marked angulation at the lower third of the tibia, with cyst formation higher in the bone. The cyst eventually healed and was followed by another cyst in a different place. There were typical sclerosis and narrowing of the medullary space in the lower half of the bone. In spite of careful protection with casts and braces, fracture finally occurred at the age of 2½ years and progressed to

This report of progress is compiled from a review of 120 articles selected from 152 titles dealing with orthopedic surgery which appeared in the medical literature approximately between Nov. 1, 1939 and March 1, 1940.

1. Scott, C.: Am. J. Roentgenol. **42**:104, 1939.

pseudarthrosis. The author feels that this condition is a form of congenital localized osteitis fibrosa cystica, with a poor blood supply at the point of fracture. Little is known about its early development.

[ED. NOTE: According to our experience, cyst formation is common but is not seen in every case.]

Claw Foot.—A study of 152 patients suffering from claw foot is presented by Hallgrimsson.[2] There were 58 male and 94 female patients. Symptoms of this deformity commonly appeared between the ages of 11 and 20 years. Fifty-three of these patients were given a careful neurologic examination. Thirty-one had neurologic symptoms, and 21 had spina bifida. The author did not believe that spina bifida and congenital myelodysplasia were of etiologic importance. The data pointed to a slowly developing lesion of the central nervous system. The exact nature of the nervous disorder was difficult to determine, since symptoms usually did not appear until adolescence. Symptomatic treatment was commonly given. The author favors transplantation of the peroneal tendons rather than cuneiform osteotomy. About six months is required for the weight of the body to flatten and lengthen the arch of the foot.

[ED. NOTE: The results of tendon transplantations for this deformity are discouraging. Osteotomy when growth is almost complete is the most satisfactory treatment.]

Fusion of the Cervical Portion of the Spine in Congenital Torticollis.—Giutini[3] reports 2 cases of congenital torticollis with fusion of the second and third cervical vertebrae. This partial fusion induces a homologous deviation of the cervical portion of the spine. Careful roentgen study in all cases of congenital torticollis will help in classification of such anomalies and is important for prognosis and cure. A review of the literature is given.

Late Results of Closed Reduction of Congenital Dislocation of the Hip.—Deutchländer,[4] of Hamburg, Germany, reports 4 cases of congenital dislocation of the hip in which the patients were followed for many years. In the first the dislocation was reduced when the patient was 2 years old and was followed for twenty-eight years. While there is no pain or functional disturbance referable to the dislocation, roentgenograms show extensive degenerative changes in the hip which cannot be differentiated from hypertrophic arthritis. In the second case the patient underwent reduction of a congenital dislocation at the age of 3 years. The appearance twenty-nine years later was that of marked

2. Hallgrimsson, S.: Acta orthop. Scandinav. **10**:73, 1939.
3. Giutini, L.: Chir. d. org. di movimento **24**:519, 1939.
4. Deutchländer, K.: Ztschr. f. Orthop. **70**:38, 1939.

deformity of the femoral head and of the acetabulum. In the other 2 cases the patients, with reduction performed at the ages of 2 and 3 years respectively, showed similar changes in the roentgenograms. Functional disturbances were not observed. At these ages, however, anatomic restoration of the hip probably does not occur, since this is a biologic deformity and not a true dislocation.

DEVELOPMENTAL DISEASES OF BONE

Marble Bones.—Kramer and his associates [5] made a chemical analysis of bone from an infant aged 4½ months with marble bones and rickets. They compared their findings with analyses made on the bones of an 18 week fetus, a 5½ hour infant, a 6 day infant, a 10 year old girl and a 29 year old man, none of whom had marble bones. They made determinations of the values for calcium, phosphorus, magnesium, carbon dioxide, water and fat. The percentages of ash, calcium and phosphorus were higher in the case of the infant with marble bones. The ratio of residual calcium to phosphorus was in harmony with the idea that the calcium-phosphorus compound in marble bones is tertiary calcium phosphate. They found a high carbonate content and hypermineralization. The high carbonate content was also present in adult and in rachitic bone and may account for the increased fragility. Hypermineralization is not associated with rickets. Hence the authors conclude that high carbonate content and hypermineralization characterize the mineral content of marble bones.

Madelung's Deformity.—Thompson and Kalayjian [6] present 4 cases of Madelung's deformity with photographs, line drawings and roentgenograms. This clinical entity, first described by Madelung in 1878, is a disturbance in growth, in most instances bilateral. It develops spontaneously, never before the age of 13 years and rarely after the age of 23. The authors state the belief that retardation of the rate of growth must precede premature closure of the growth plate of the radius if one is to account for the curvature in the diaphysis. Pain occurs only when the deformity is sufficient to distort or distract the distal radioulnar articulation. Premature closure of the radial epiphysial line of growth occurs, while the ulna continues to grow and projects dorsally and distally from the subluxated carpus and hand. The clinical symptoms consist of pain and limited motion in the carpus and the distal radioulnar articulation. The hand deviates to the ulnar side. The prominent distal end of the ulna may be replaced manually to the level of the wrist but returns to its dorsal position when pressure is released. Treatment,

5. Kramer, B.; Yuska, H., and Steiner, M. M.: Marble Bones: Chemical Analysis of Bone, Am. J. Dis. Child. **57**:1044 (May) 1939.

6. Thompson, C. F., and Kalayjian, B.: Surg., Gynec. & Obst. **69**:221, 1939.

including epiphysial arrest and later resection of a portion of the diaphysis of the ulna near the wrist, was successful in obtaining a joint free from pain. Corrective osteotomies at the points of greatest curvature after completion of growth in both bones reduced the deformity and increased the function of the wrist and hand.

TUBERCULOSIS

Tuberculosis of the Knee in Childhood.—McKeever [7] discusses the treatment of tuberculosis of the knee joint in infancy and childhood. Forty-seven patients under 10 years of age with proved tuberculosis of the knee were studied to determine the results of conservative and of operative treatment. Surgical treatment was described as removal of articular cartilage to produce bony ankylosis between the tibia and the femur. All other procedures were considered conservative (traction, casts, braces, synovectomy, excochleation, sympathectomy and extra-articular fusion). Conservative treatment for one to nine years, an average of three years for 46 patients, did not result in any case in a knee which did not show clinical signs of active disease. One child was cured by excochleation of a tuberculous abscess in the tibial epiphysis. Two died under conservative treatment. Thirty-nine patients were subjected to "economical resection" aimed at producing femorotibial synostosis. Two died as a direct result of the operation. Thirty-four were followed, and 90 per cent were in excellent health. Thirty-three, 97 per cent, of the resected knee joints were solid clinically and roentgenographically; 3 patients required two operations, 2 required three operations and 1 required four operations before fusion was accomplished. A detailed account is given of disturbances of growth and directional aberrations in a follow-up which ranged from one and a half to thirteen years.

Tuberculosis of the Knee Joint.—Toumey [8] reports 222 cases of tuberculosis of the knee joint in which fusion of the knee was performed in the period from 1915 to 1936. One hundred and ninety-nine of the patients were followed from one to seventeen years after operation. Fusion occurred in 196, or 98 per cent. Fixation in plaster was stopped at an average of eight months after operation. The disease subsided in all but 7 patients, in whom sinuses persisted, and in no fused knee did tuberculosis recur. Fifty-nine patients were 10 years of age or less at the time of operation, and 14 were 5 years old or less. The diagnosis was made when flexion deformity, synovial thickening and marked atrophy of the thigh and calf were present, but it could not be proved

7. McKeever, F. M.: Tuberculosis of Knee in Infancy and Childhood, J. A. M. A. **113**:1293 (Sept. 30) 1939.

8. Toumey, J. W., Jr.: Surg., Gynec. & Obst. **68**:1029, 1939.

except by exploration of the joint and verification by laboratory methods. In 146 cases of the series the diagnosis was proved by the observation of tubercles in the sections. The most common presenting complaint was swelling at the knee; the next, pain, and the next, stiffness. Roentgen examination revealed overdevelopment of the epiphyses in frequent instances. After the fusion operation, adult knees were put up in 10 degrees of flexion, as the gait was better with that position, while those of children were placed in 180 degrees of extension. Use of a plaster cast was continued until solid fusion had occurred. There were 14 patients in this series who were 5 years old or less at the time of the fusion operation, the youngest being 2 years of age. Solid bony fusion was obtained in every case in this group; 6 of the patients have been followed from eight to fourteen years.

Tuberculosis of Tendon Sheath.—Tuberculosis of the serous bursae about the hand is an uncommon complication of tuberculous infection. Potts [9] reports 2 cases in detail. Infection in both instances followed trauma. The pathologic process varies with the duration of the disease. At first there is simple synovitis. Later the synovial sheath is congested with reddened elevations, and at this stage tubercles may be found. Adhesions commonly occur. The tendon may become frayed and necrotic. The symptoms are those of a slow progressive swelling followed by stiffness and occasionally tenderness. A sinus may form. The characteristic lesions produced by tubercle bacilli must be found to establish the diagnosis. Treatment consists of care in a sanatorium and rest of the part. Roentgen therapy has been helpful. Surgical extirpation may be considered if removal of the diseased tissue will not interfere with future function of the hand.

OSTEOMYELITIS

Complications of Osteomyelitis.—Hobart and Miller [10] have observed 17 cases of carcinomatous degeneration of the skin associated with chronic osteomyelitis in a series of 4,796 cases of the latter condition. They report in detail 7 cases of carcinoma and 2 cases of "toxic deafness of the eighth nerve" complicating osteomyelitis. The age of the patients in the group with cancer varied from 52 to 73 years; the duration of the infection was from one and one-half to fifty years. The lesions were all in the lower extremities, in 6 cases below the knee, and in 1, in the thigh. The symptoms were a chronic discharge, slight local pain, a foul odor and (in 3 cases) hemorrhage. In 5 of the 7 cases amputation was done; in 1 a wide curettement with an Orr petrolatum pack was done, and 1 patient died before the necessary operation could

9. Potts, F. N.: New York State J. Med. **39**:983, 1939.

10. Hobart, M. H., and Miller, O. S.: Am. J. Surg. **45**:53, 1939.

be performed. No recurrence or metastasis has been observed in any of the remaining 6 patients in a follow-up of one to three years. The roentgenograms revealed nothing characteristic of malignant invasion of soft tissues but in some instances showed suspicious moth-eaten areas with rarefaction. The histologic picture in 6 instances was that of squamous cell carcinoma; in the seventh the pathologic tissue was diagnosed as sarcoma.

Present Status of Chronic Osteomyelitis.—McCarroll and Key[11] describe 200 consecutive cases of chronic osteomyelitis. Forty-one of the patients had been treated for more than one week with an erroneous diagnosis during the acute stage of the process. In only 9 was the bone drained during the first week of the disease. Consequently, about 191 of these patients had been treated conservatively or by delayed operation. In this entire series the incidence of secondary osseous foci was 25 per cent, and that of involvement of the neighboring joint was 50 per cent. By means of standard surgical procedures and prolonged hospitalization with adequate after-treatment it was possible to obtain healing in only 61.3 per cent of 98 patients who were followed for three years or longer. In 38.7 per cent of these the sinuses continued to drain or the disease healed and recurred during the period of observation. Of their series of 200 cases the authors consider their end results poor in 35.5 per cent, fair in 28 per cent, good in 25.5 per cent and unknown in 11 per cent. In conclusion they state the belief that cure of the disease depends on the ability of the surgeon to perform an adequate operation and remove all of the infected bone and that the type of after-treatment is relatively unimportant provided adequate drainage is maintained. Forty per cent of the patients in whose cases adequate surgical treatment was not feasible remained practically incurable. Furthermore, the authors express the opinion that early diagnosis of acute hematogenous osteomyelitis and prompt draining of the focus in the bone are the most important factors in prevention of chronic osteomyelitis and its attendant economic waste and crippling. The actual treatment is as follows: The operation is performed under a tourniquet when one can be used. After wide saucerization is completed, the wound is packed with dry, fine mesh gauze in order to control bleeding, and a dry dressing is applied. A cast is not applied unless there is danger of a fracture of the residual shaft or of the involucrum. On the third postoperative day the gauze pack is removed with the patient under nitrogen monoxide and oxygen anesthesia, and a petrolatum gauze pack is inserted. This is changed at intervals of from two to four days. After the first two or three dressings the wound is lined by granulation tissue, and little pain is experienced by the patient. If at any time the granulations do not appear healthy,

11. McCarroll, H. R., and Key, J. A.: Surg., Gynec. & Obst. **68**:1007, 1939.

wet dressings are used and the wound is irrigated with physiologic solution of sodium chloride for a few days. Petrolatum gauze is then substituted. In addition, the Carrel-Dakin method and various types of wet dressings have been used.

[ED. NOTE: This gloomy picture of the result of treatment of chronic osteomyelitis shows that there is great need for further investigation of this disease. In this review a number of the newer procedures, such as chemotherapy, toxin therapy and roentgentherapy are not mentioned.]

CHRONIC ARTHRITIS

Orthopedic Treatment of Strümpell-Marie Arthritis.—Swaim's [12] report is based on the study of 106 cases of advanced spondylitis extending over a period of twenty-two years. There were 22 female and 84 male patients. The deformity in this disease presents itself as a long bend of the whole spine, with a reverse curve in the lumbar region, so that in standing the pelvis is actually tipped backward and constant strain is thrown on the hip joints. Involvement of the hip appears to be secondary to the strain induced by bad posture and loss of normal lordosis. Rarely, lateral curvature is produced by unequal spasm. The progress is slow, and, except for the hips, rarely attacks the extremities except in women. The treatment adopted by the author is as follows: First, the posture is improved by recumbency. If the spine is not corrected in two weeks, a jacket is applied. The patient is placed on a Goldthwait frame, which is bent to produce lordosis. Then a light plaster jacket, well padded over the spine, the anterior superior spines of the ilium and the sternum, is applied. The jacket is molded tightly over the abdomen to limit abdominal breathing, to force the chest up and to compel expansion of the upper part of the chest. It is left high in front and cut just below the shoulder blades in back, so that with each breath the chest is forced against the jacket in front, thus straightening the thoracic portion of the spine. The jacket extends to the symphysis in front and the tip of the spine in back and grips the pelvis firmly. There must be no space below the jacket in front which will permit abdominal breathing. Most of the patients are more comfortable when held firmly, and they dread having the jacket removed. The jacket is kept on uninterruptedly for several weeks, until all spasm has gone. Then a new jacket is made. Plaster jackets are applied until the best possible correction has been obtained. Then a more permanent leather jacket is made. Although 62 patients have worn jackets, the author chooses only 23 cases from which to draw conclusions, because in these the jackets have been worn for from four to nine years. Of the 23 cases, the good posture thus obtained was maintained in 5, improved in 15 and

12. Swaim, L. T.: J. Bone & Joint Surg. **21**:983, 1939.

lost in 3. One of the patients refused the jacket after two years; 1 cut his jacket in front, so that it no longer supported, and 1 was uncooperative. No trouble with the hip developed in any of the 62 cases. In the group of 23 patients who wore jackets from four to nine years, 11 had symptoms referable to the hip at the beginning, and 7 of these became completely symptomless; the 3 patients with fused hips showed no change; 1 patient became unaccountably worse. Expansion of the chest decreased in 7, was unchanged in 2 and increased in 14 patients. Weight increased in 20, remained the same in 2 and decreased in 1. Sixteen patients are working; 6 are at home, unemployed but looking for work, and 1 died of carcinoma of the breast. In 13 cases some ossification of the ligaments was present before the jackets were used, and in these cases the bridging increased in spite of the jackets. Seven of the 23 patients showed no bridging at first, but later 4 of these had one or two bridges, usually at the twelfth thoracic or the first lumbar vertebra. Three of the 7 showed no bridging, even at the end of four, five and eight years respectively. Although there are too few cases and the period for which the jackets were worn is too short to enable one to draw final conclusions regarding prevention of ossification, this study strongly suggests that ossification is much less rapid in patients treated with jackets. Excellent photographs accompany the text.

SPINE

Persistent Epiphyses of the Vertebral Process.—Bailey [13] has found that secondary centers of ossification may appear opposite the tips of any of the major vertebral processes. The transverse processes regularly have secondary centers. The inferior processes frequently have them, and they occur occasionally in the superior articular processes and in the spinous processes. These secondary centers may persist into adult life and are frequently confused with fracture. Ossification of a vertebra begins at the age of 8 weeks in three centers, one for the body and one for each half of the neural arch. A ringlike center of ossification develops at the periphery of the cartilaginous plates at each extremity of a vertebra at about the seventeenth year and fuses with the body of the vertebra at about the twentieth year. This ringlike center is seen in profile in a lateral view as a small triangular piece of bone. Differentiation of persistent epiphyses in the vertebrae from fracture can usually be made. Ordinarily there are severe pain and disability from fracture, and fracture fragments are usually more displaced. A fracture line is serrated, while an epiphysial line is smooth, and the epiphysis has a definite cortex parallel to a cortex on the opposing surface. A final point is that persistent epiphyses are often multiple or bilateral.

13. Bailey, W.: Am. J. Roentgenol. **42**:85, 1939.

Pain Low in the Back Caused by Protrusion of the Intervertebral Disk.—Craig and Walsh [14] discuss pain low in the back and sciatic pain resulting from protruded intervertebral disks and hypertrophied ligaments. The cause of this condition is probably traumatic, and the trauma may produce injury to other structures. Thus, it was found that of the 175 patients with herniated intervertebral disk most recently observed, 155 had an associated hypertrophy of the ligamenta flava. Statistical analysis of the cases of 300 patients in whom protrusion of the intervertebral disks was verified at operation reveals the following data: 1. The 300 cases in which a diagnosis of probable protruded disk had been made were selected from approximately 10,000 cases of pain in the lower part of the back and sciatic pain observed in three years. Three hundred and thirty-two protrusions were found in these 300 cases. There were protrusions in the lumbar region in 285 cases and in the cervical and thoracic regions in 15. In 270 cases the protrusions were single, and in 30 cases they were multiple. Thirty were at the third lumbar interspace, 140 at the fourth lumbar interspace and 139 at the fifth lumbar interspace. Of the 300 patients, 226 were men and 74 were women. The average age at operation was 40 years. One hundred and seventy-six (59 per cent) gave a history of injury. In 37 per cent of the cases the patient recalled that injury immediately preceded the symptoms. In 81 per cent there was intermittence of symptoms. Unilateral sciatic pain was the most common symptom; bilateral sciatic pain occurred in 15 per cent of the cases. In 174 cases the value for protein in the spinal fluid was 40 mg. or more per hundred cubic centimeters; in 91 cases it was below 40 mg. There were no deaths in the series. In no case was it necessary to do a fusion operation to relieve postoperative pain.

SHOULDER

Calcification of the Supraspinatus Tendon.—Bishop [15] studied calcareous deposits about the shoulder and found that they are more common than is generally believed. One fourth to one third of the patients showed deposits in both shoulders, only one shoulder being symptomatic at the time of examination. Calcification in the supraspinatus tendon usually occurred between the thirtieth and the fiftieth year. The tendon of the supraspinatus muscle reenforces the central portion of the capsule and is inserted into the anterior and uppermost part of the greater tuberosity. The thin synovial lining of the subacromial bursa is tightly adherent to the tuberosities and to the adjacent part of the conjoined tendons. Bishop discusses the etiology and feels

14. Craig, W. McK., and Walsh, M. N.: Minnesota Med. **8**:334, 1939.

15. Bishop, W. A., Jr.: Calcification of Supraspinatus Tendon: Cause, Pathologic Picture and Relation to Scalenus Anticus Syndrome, Arch. Surg. **39**:231 (Aug.) 1939.

that repeated minor traumas may cause rupture of a few fibers of the tendon. Repeated tearing and healing lead to areas of hyaline degeneration and finally to deposition of calcium. The calcium is located at the base of the bursa, usually in relation to the supraspinatus tendon but occasionally associated with the subscapularis tendon and, less frequently, the infraspinatus tendon. Occasionally the onset of symptoms is abrupt and viciously painful, but usually a history of an insidious onset with an uncomfortable feeling associated with certain movements of the shoulder can be obtained. Pain was grouped into three types: (1) pain localized at the point of insertion of the deltoid muscle; (2) constant dull and boring or aching pain near the tip of the shoulder at the point of greatest tenderness, and (3) almost intolerable pain in the muscles of the neck, in the scapular region and occasionally down the arm to the finger tips. This is probably due to reflex spasm of the scalenus anticus muscle of the affected side. The diagnosis depends on careful history taking, physical examination and roentgen examination. A case is presented to illustrate the types of pain encountered. Treatment of acute conditions is by immediate lavage. Subacute or chronic conditions are treated by diathermy or lavage. A small percentage of the patients require surgical removal of the deposit.

Lesions of the Supraspinatus Tendon.—Horwitz [16] reviews the pathologic observations in 150 shoulders of 75 cadavers with an average age at death of 55 years. Bursal changes were noted in 30 specimens. These alterations consisted of thickened walls, villus formation and partial or complete obliteration of the cavity. In 10 of the shoulders there were communications between the bursa and the joint, due to a tear of the supraspinatus tendon. There were 10 complete tears of the musculotendinous face, of which 3 were bilateral and 4 were unilateral. The youngest subject in these cases was 50 years of age. In 49 shoulders there was a variable amount of thinning of the cuff, and in 30 instances the superficial surface was frayed and fibrillated. Constriction in the biceps tendon in the groove was seen. In 75 shoulders varying stages of flattening, thinning, fraying and fibrillation were evident. In 4 cases complete tears were noted, with reattachment of the distal portion of the tendon to the region of the lesser tubercle. In 1 case the tendon was bound down by adhesions. The bony changes were proportional to the alterations in the soft tissue. Bony recession and atrophy of the greater tubercle were found in the cases in which complete tears of the tendon had occurred. Occasionally the joint cartilage was denuded in areas. The author feels that rupture of the supraspinatus tendon represents the

16. Horwitz, M. T.: Lesions of Supraspinatus Tendon and Associated Structures: Investigation of Comparable Lesions in Hip Joint, Arch. Surg. **38**:990 (June) 1939.

effects of trauma, often minimal, on tissues which are the site of degenerative lesions incidental to advancing age, defective circulation, excessive use and attritional changes. Trauma serves merely to hasten the progress of pathologic events already taking place. The wisdom of subjecting the patients to surgical procedures is therefore to be questioned. This does not apply, however, to patients who have not reached the fourth decade of life.

KNEE

Injuries to the Meniscus.—Efskind [17] reports the end results of 36 operations for injury to the semilunar cartilage performed between 1928 and 1936. At operation 32 torn cartilages were found. One patient had cysts in the cartilage, and in 3 instances nothing abnormal was found. All but 2 of the patients have been followed by the author to the present time. In 40 per cent the knee is functionally and anatomically normal. All of these patients have returned to their regular work except 20. Diminution in the joint space where the cartilage was removed was common. Abnormal static changes occurred with defects in the articular cartilage in 13 patients, without any change in the knee not operated on. Occasionally there were changes also in the synovial membrane and fat pad.

Injuries to the Knee in Athletics.—Hopkins and Huston [18] studied the end results of 193 severe injuries to the knee. All of the patients were young men attending Springfield College. There were 19 patients with traumatic synovitis. In only 1 case was aspiration performed. Support of the knee with a bandage was the usual treatment. A satisfactory end result was obtained in 17 cases, an average period of four weeks being required for complete recovery. In 2 patients there were recurrent pain and swelling after exercise. In 59 patients a strain of the lateral ligament occurred; in 54 of the internal ligament, and in 5, of the external ligament. Treatment consisted of crutches, tight bandage and physical therapy. The average time lost from athletics was three weeks. While immediate recovery appeared to be good in all but 4 cases, less than half of the patients have remained free from symptoms. The chief complaints are of pain and swelling with vigorous use. The writers suggest that there may have been an associated injury to the semilunar cartilage which could not be demonstrated at the time of injury. There were 139 injuries to the semilunar cartilages. Fifty-three of these were treated by rest, support and physical therapy. Thirteen required removal of the cartilage later. Treatment by rest, support and physical therapy gave good end results in only 19, or 36 per cent. In 24 cases of injury to the semilunar cartilage a plaster cast

17. Efskind, L.: Acta chir. Scandinav. **82**:499, 1939.

18. Hopkins, F. S., and Huston, L. L.: New England J. Med. **221**:95, 1939.

was worn for an average of four weeks, and crutches were used. The end result was good in 18, or 66 per cent. Eleven patients originally treated by immobilization in plaster required operative removal of the cartilage later. There were 22 patients with probable injury to the semilunar cartilage. An exact diagnosis could not be made. All of these were treated with rest and support to the knee. Seven still have slight disability. The authors feel that immobilization should be tried in all cases of injury to the semilunar cartilage before operation is resorted to.

[ED. NOTE: In cases of severe injury to the knee an exact diagnosis often cannot be made immediately. In such instances prolonged support is indicated until the extent of the injury can be determined.]

Treatment of Weak Feet.—Graham [19] divides weakness of the feet into three types: (1) that due to postural deficiencies, (2) that resulting from a shortened achilles tendon, and (3) that due to anatomic deformities of the bones. He states that in the condition due to postural faults a valgus of the posterior part of the foot occurs from an attempt to adjust to the line of gravity, which in faulty posture with increased forward inclination of the pelvis comes anterior to the acetabulum. To bring the weight thrust anterior to the acetabulum the femoral column rotates internally. Since no rotation is possible at the knee or ankle, this rotation must take place at the subastragalar joint, with resulting valgus. The anterior part of the foot follows the os calcis into eversion and abduction. This rotatory movement is increased as the astragalar head moves medialward. As the os calcis is tilted, the astragalus becomes more depressed, with lowering of the inner side of the foot. With locomotion a relative dorsiflexion of the anterior part of the foot and hypermobility of the first metatarsal segment occur and are followed by splaying of the front portion of the foot. A relative break occurs in the midsection of the foot, and this may be followed by abduction and supination of the anterior portion. A short achilles tendon may be compensated by high heels, with marked diminution of function in the mediotarsal joints. With low heels, valgus results in an attempt to bring the heel to the ground. In his discussion of weakness of the feet due to anatomic deformities the author mentions shortness of the first metatarsal bone and the posterior location of the sesamoid bones beneath it. The metatarsal bone extending farthest forward must act as the principal fulcrum. When the second metatarsal is longer than the first, the foot becomes pronated and abducted to permit functional use of the first metatarsal bones. In treatment of weak feet the causes must be eliminated, particularly with the first and second types. In cases of acute involvement with synovitis and

19. Graham, J.: Illinois M. J. **75**:425, 1939.

myofascitis the author advises rest with the foot fixed in varus. Supports are worn for four to six weeks. They are then gradually discarded, and the threshold of muscular fatigue is raised by exercise.

[ED. NOTE: This careful analysis of the mechanics of weak feet is commendable. In most cases the use of supports and muscular reeducation must be continued for longer periods than are suggested in this article.]

NEOPLASMS

Angioendothelioma of Bone.—A brief review of the knowledge of this type of tumor is given by Lutz and Pusch.[20] Clinically the growth does not differ from other forms of sarcoma. Growth is rapid, and pulsation may be present. The tumor is generally solitary. Roentgen examination shows a bulky cystlike formation with fine lacelike trabeculae throughout. The wall is defined and has a tendency to blend with the soft tissues. Marked destruction of bone is present without production of bone. The growth often resembles a giant cell tumor. It has been seen in the long bones, ribs, pelvis and vertebral column. It is somewhat radiosensitive. Metastases are commonly found in the lungs. Microscopically the tumor is characterized by blood-filled tubular columns of cells with bulky clear cytoplasm. A case of angioendothelioma of the humerus in a woman aged 54 is presented in detail.

Xanthomatous Tumors of Joints.—De Santo and Wilson [21] present a complete study of this interesting condition, including 9 case histories with photographs, roentgenograms and photomicrographs. Xanthoma of the synovial membrane of the joints is probably more common than has been hitherto supposed, as is exemplified by this group of 9 cases collected in a brief period. The preoperative diagnosis of articular xanthoma seems never to have been made. Obscure intermittent swelling of the knee joint associated with pain and free fluid, occasional locking and a movable tumor, usually medial to the patella, frequently are caused by xanthoma. Aspiration of the joint with recovery of dark or sanguineous fluid points to the presence of tumor. The demonstration of a large amount of cholesterol in the fluid is probably pathognomonic of xanthoma. Xanthoma originates in chronic hemorrhagic villous arthritis. The stroma cell is related to the reticuloendothelial system. It is derived from the surface mesothelium of the synovial membrane, which has reticuloendothelial properties, and gives rise to: (*a*) the foam cell, (*b*) the giant cell and (*c*) the pigmented cells associated with xanthomatous disturbance of lipoid metabolism. The value for blood cholesterol is frequently elevated. Cholesterol formation

20. Lutz, J. F., and Pusch, L. C.: Angio-Endothelioma of Bone, J. A. M. A. **113**:1009 (Sept. 9) 1939.

21. De Santo, D. A., and Wilson, P. D.: J. Bone & Joint Surg. **21**:557, 1939.

probably takes place locally as a result of interstitial hemorrhage, and the cholesterol is a product of decomposition of hemoglobin. Its failure to be formed universally when interstitial hemorrhage occurs is partially explained by the systemic disturbance of lipoid metabolism which usually exists. Xanthoma of a joint can be cured by radical excision. In the case of a solitary tumor local excision is sufficient, but in the case of multiple or diffuse xanthoma subtotal or total synovectomy is usually necessary. No instance of a benign giant cell xanthoma undergoing malignant transformation was found.

MISCELLANEOUS

Traumatic Fat Embolism.—Whitaker,[22] discussing traumatic fat embolism, states that the chief source of fat is injured bone and that the fat is drawn or forced by compression into torn haversion canals, which do not collapse as veins do elsewhere when torn across. Pressure exerted by extravasation of blood and serum into tissues tends to force liberated fat into the veins. If a cast is applied before maximum swelling of tissues is reached there is a tremendous increase in this pressure. The fat goes to all parts of the body, but the symptoms are usually referable to the lungs and the brain. Two cases are presented, in 1 of which there were pulmonary, in the other profound cerebral, signs and symptoms. Both patients made complete recovery. A petechial rash and detection of fat in the urine are helpful diagnostic signs. Treatment is symptomatic. More can be done to prevent than to treat fat embolism, and one of the most important points is careful handling and manipulation of injured bone.

Gas Gangrene in Civil Life.—In an editorial [23] in *The Journal of the American Medical Association* it is stated that the death rate from gas gangrene is still appallingly high. In Millar's series of 607 patients in civil life there was a mortality rate of 49.7 per cent, while the mortality from the same infection in the American Expeditionary Forces in France was 48.52 per cent. Eliason, in 349 cases of gas gangrene following amputation for arteriosclerotic or diabetic gangrene, recorded a mortality of 59 per cent for the entire group and 75 per cent for diabetic patients. In a group of cases in which operations other than amputations were performed the mortality was 41 per cent with serum and 76 per cent without serum. Two facts largely responsible for the lack of awareness of gas gangrene by physicians are (1) that gas

22. Whitaker, J. C.: Traumatic Fat Embolism: Report of Two Cases with Recovery, Arch. Surg. **39**:182 (Aug.) 1939.

23. Gas Gangrene in Civil Life, editorial, J. A. M. A. **113**:234 (July 15) 1939.

gangrene is rare in time of peace and (2) that it always presents itself in the typical grave form. Gas gangrene is caused almost exclusively by anaerobic bacilli. Deeply lacerated, contused, soiled wounds, compound fractures, hematoma and interference with blood supply create favorable conditions for the growth of anaerobes. The local signs are rapidly increasing swelling, serous or serosanguineous discharge, mottled discoloration of the skin, crepitation of tissues and escape of gas from the wound with the characteristic odor. Early roentgenograms showed gas deep in the tissues. Serum is definitely indicated for both prophylaxis and treatment. Judgment as to sulfanilamide and roentgen therapy must be suspended until further experience is obtained.

Gas Gangrene.—Newell [24] reviews the diagnosis and the present day treatment of gas gangrene. About twenty-five varieties of anaerobic organism have been isolated, the chief ones being Clostridium welchii, Clostridium oedematis maligni (vibrion septique) and Clostridium oedematiens. The diagnosis rests mainly on severe pain, a high pulse rate, edema and brownish discoloration of the skin. There may be a mousy or putrid odor or no odor. Roentgenograms may show gas bubbles in the tissues, and subsequent ones taken at four hour intervals demonstrate an increase in the number of bubbles. Crepitus of the tissues is a relatively late finding. If the infection is due to vibrion septique, there will be only edema and no gas formation. In regard to treatment, it is generally concluded that the prophylactic injection of gas antitoxin does not prevent gas infection but that it probably lengthens the incubation period and lessens the severity of the attack. Polyvalent gas antitoxin in doses of 10,000 to 30,000 units should be administered intravenously every six to eight hours. Roentgen therapy is a definite aid in treatment, but it seems desirable to use serum with it. For local use, dilute solution of sodium hypochlorite, hydrogen peroxide or 1 : 500 potassium permanganate solution is indicated. Sulfanilamide has been used recently, and the results have been encouraging.

Dislocation of the Extensor Tendons in the Hands.—Straus [25] reports that dislocation of the extensor tendons in the hands is a rare injury. There are immediate disturbance of function and swelling of the dorsum of the hand. The swelling soon subsides, but interference with extension is permanent unless it is repaired. The author reports in detail the history of a case of dislocation of the extensor tendon at the third metacarpophalangeal joint. Operative exploration showed a V-shaped tear in the tendon permitting the intact lateral half of the tendon to slide to the ulnar side. The tear was sutured, and a reten-

24. Newell, E. D.: Ann. Surg. **110**:100, 1939.
25. Straus, F. H.: Ann. Surg. **111**:135, 1940.

tion slip of fibrous tissue was turned over the tendon from the ulnar side and sutured to the soft tissues on the radial side. Normal function was regained after this procedure.

Kienböck's Disease of the Carpal Navicular Bone.—Cave [26] states that fewer than 100 cases of this lesion have been recorded in the literature. At the Massachusetts General Hospital the diagnosis has been made 5 times. In regard to etiology, it is generally agreed that severe trauma is not necessary to produce necrosis of the carpal navicular bone, but in the majority of the cases trauma is present. Trauma results in tearing of the dorsal ligament and subsequent interruption of the blood supply followed by aseptic necrosis of the bone. In 1 of the author's cases microscopic examination showed an extensive necrotic process subjacent to the articular cartilage. There was an occasional focus of apparent new bone formation. Several groups of foreign body giant cells were observed. The diagnosis depends on the roentgen findings. In the anteroposterior view one may see early cyst formation and irregularity of the radial surface, with localized areas poor in calcium and other areas with marked increase in the calcium content. As the disease progresses the bone becomes dense, smaller and irregular in outline, taking on the appearance of a sequestrum. In the lateral roentgenograms the density of the bone is increased. The disease commonly occurs in young men who do heavy work. There is a history of slow but definite increase in pain, moderate stiffness and thickening of the wrist joint. Thickening is most marked over the dorsum, in the central portion. Local tenderness is usually acute and is sharply localized to the center of the dorsum of the wrist. In the acute stage, active motion in any direction may be painful. If the diagnosis is made early, conservative measures, consisting of support from a plaster or leather wristlet, may help to restore nutrition to the bone and prevent advance of the process. When the bone is permanently deformed, however, and has the appearance of an irregular sequestrum, or when it has disintegrated, the treatment is excision, with great care to avoid trauma to surrounding structures. Good recovery of function in the wrist joint, with little or no pain, may be expected after the diseased lunate bone has been removed.

FRACTURES

Resection of the Radial Head and Neck.—After a study of 13 cases of resection of the radial head and neck King [27] reports the end results as follows: in 1 case, excellent; in 5, good; in 4, fair, and in 3, poor. One of the chief factors which cause disability is bone formation at the operative site. The author feels that this may be minimized if the fol-

26. Cave, E. F.: J. Bone & Joint Surg. **21**:858, 1939.
27. King, B. B.: J. Bone & Joint Surg. **21**:839, 1939.

lowing points are stressed: 1. Complete removal of all free or loosely attached bone fragments, periosteal shreds or strips and capsular tissue at the time of resection. 2. Avoidance of stripping back the periosteum from the radial stump unless the stripped-up portion of the periosteum is completely excised or sutured over this stump to form a limiting membrane. 3. Use of a free graft of fascia lata snugly approximated with purse string sutures over the end of the radial stump to form a limiting membrane, in case the periosteum has not been so used. Another factor which causes disability is proximal displacement of the radial shaft, which may be prevented, as was suggested by Key and Conwell, by snugly approximating the soft tissues with several interrupted purse string chromic catgut sutures to fill in securely the dead space created by removal of the radial head and neck. The annular ligament should be repaired. It is probably of value to immobilize the wrist in maximum ulnar deviation for two or three weeks after resection of the radial head and neck, in order to allow the formation of scar tissue to obliterate further the dead space which was closed in with interrupted purse string sutures. After operation a plaster cast should be applied from the bases of the fingers to just below the elbow, which allows free pronation and supination. The arm is supported in a sling; the elbow is flexed to a right angle, with relaxation of the biceps. After removal of the cast, "daily active and passive ulnar deviation stretching exercises" are in order. The author feels that resection of the radial head should be avoided if possible in the growing child and in the adolescent, because a marked degree of calcification and bone formation frequently follows operative or traumatic insults to this region in the growing child. Four of the 5 patients in this group who showed no appreciable bone formation following resection were 21 years of age or older.

Ununited Fractures of the Carpal Navicular Bone.—Edelstein[28] reports 6 cases of ununited fracture of the carpal navicular bone seen from three months to nine and one-half months after injury. In each case bony union resulted from a bone-drilling operation, which he describes. He states the opinion that when sclerosis is present between the fragments in an old fractured navicular bone union will not take place. Instead, severe arthritis supervenes and becomes progressive, involving the immediately neighboring intercarpal joints and the radiocarpal joint. The navicular bone possesses little periosteum to assist in the formation of subperiosteal callus. The formation of bone in the callus is slower than in other fractures, owing to the poor blood supply. The bone has only a small surface posteriorly and anteriorly for the attachment of ligaments. Elsewhere it is covered with cartilage. Its

28. Edelstein, J. M.: J. Bone & Joint Surg. **21**:902, 1939.

blood supply is derived from two vessels, one of which penetrates the tuberosity. Therefore, a fracture through the waist of the bone renders the proximal fragment avascular. Because of the poor blood supply, union takes a long time, for the vessels have to grow from the peripheral into the central fragment. These fine capillary vessels are ruptured with the slightest shearing movement; hence the necessity for complete immobilization. With adequate and early immobilization nonunion should never occur.

Treatment of Obstetric Fractures of Femur.—For obstetric fractures of the femur Pavlik [29] advises reduction of the fracture and retention of the limb in abduction by means of a plaster of paris cast symmetrically applied to both lower extremities in a similar manner to the application of a cast for the treatment of congenitally dislocated hips. The treatment has the advantage of simplicity. It does not require hospitalization. During the first month the plaster is changed each week; the final bandage is worn for one month, and treatment is usually terminated at the end of two months, at which time the callus is sufficiently strong. This method has been used for the past three years. In each case the fragments have healed satisfactorily without appreciable shortening of the limb.

Excision of the Fractured Patella.—Dodd [30] gives an account of 5 consecutive cases of fractured patella treated by excision of the fragments. The operation is carried out as soon after the accident as conditions permit; if possible, on the same day. After the fragments have been removed, the quadriceps tendon is closed by interrupted thread sutures; on the seventh day after operation flexion of the knee is practiced over the side of the bed, and walking with a cane begins on the tenth day. In all 5 cases normal function was obtained.

[ED. NOTE: Occasional reports have appeared of removal of the patella, which has been regarded as a sesamoid bone. Sufficient time has not elapsed, however, to determine whether removal in any way disturbs the mechanics of the knee joint.]

Pseudofracture of the Tibia.—Roberts and Vogt [31] present 12 cases of what they consider a clinical entity involving the upper third of the tibial shaft in children between the ages of 4 and 16 years. The roentgen appearance may simulate a fracture, but the condition is not due to acute trauma. The cause is not known but may be a chronic infectious process. The pathologic reports on 2 of the patients in whose cases biopsies were done and the fact that slight fever and leukocytosis were present in 3 of the cases suggested this. It is suggested that the so-called

29. Pavlik, A.: J. Bone & Joint Surg. **21**:939, 1939.
30. Dodd, H.: Lancet **2**:130, 1939.
31. Roberts, S. M., and Vogt, E. C.: J. Bone & Joint Surg. **21**:891, 1939.

pseudofracture line may be influenced by the course of a nutrient artery. The arguments against classification of the condition as a fracture are as follows: 1. Except in 1 case, there was no history of trauma adequate to cause a fracture of the tibia. 2. Transverse incomplete fracture of the upper end of the tibia must be extremely rare in this age group, as no case could be found in the records of the fracture service of the Massachusetts General Hospital for the years 1920 to 1937, and only 1 case was observed at the Children's Hospital. 3. Roentgenograms taken within a few days of the onset of symptoms did not show any line suggestive of a fracture, but after two to four weeks or more the roentgen appearance began to suggest a fracture line. 4. The amount of subperiosteal new bone formation was greatly in excess of that which would follow even a more severe fracture. 5. Three patients had evidence of recent infection elsewhere in the body. 6. In 1 case the condition was bilateral. 7. In 1 case there was a recurrence of the disease five months after the original attack had been practically cured. All of the patients improved with rest and immobilization in plaster and eventually became free from symptoms. Others were given rest in bed followed by limited weight bearing.

ORTHOPEDIC OPERATIONS

Tendon Transplantations.—Carpenter [32] has reviewed 458 tendon transplantations performed on children. He found that 85 per cent of these operations gave satisfactory results. Poliomyelitis of over eight years' duration responded better than did poliomyelitis of shorter duration. In these cases better results were obtained with varus than with valgus deformity of the foot. Also, the transplants from tendons which arise from the larger muscles gave better results than did transplants of those from the smaller ones. It appeared to be of no advantage to wait over two years after the acute onset of poliomyelitis before performing the operation. Stabilization of the foot made the tendon transplantations more satisfactory; in fact, secondary operations for stabilization were necessary in 19 per cent of these cases when tendon transplantations had been done without primary stabilization. The type of insertion of the transplant which consists of creation of a bone tunnel and external suture appeared to be the most satisfactory procedure. An analysis of the causes of failure to obtain perfect results showed that errors in surgical judgment were more frequent than errors in surgical skill. In cases of congenital equinovarus, transplantation of the anterior tibial tendon to the mid-dorsum of the foot was the most successful procedure. Transplantation of tendons in cases of cerebral spastic paralysis and of Charcot-Marie-Tooth peroneal paralysis was not effective.

32. Carpenter, A. R.: J. Bone & Joint Surg. **21**:921, 1939.

Acetabuloplasty for Dislocation of the Hip.—Nachlas [33] describes a new technic for the shelf operation by acetabuloplasty. Through a Smith-Peterson incision the hip joint is exposed. A linear osteotomy is performed through the superior portion of the articular margin. The osteotomy extends into the hip joint. The proximal and distal ends of the osteotomized articular margin are left attached, and the margin of bone is levered laterally. The gap at the site of osteotomy is filled with bone taken from the iliac crest. The hip is put in abduction in a plaster spica for two months, and this treatment is followed by traction on the involved extremity for one month. The prime requisite for the procedure is that the head of the femur be opposite the acetabulum. This may require a preliminary period of traction or an operation to overcome contracture. The procedure was used in 8 cases. These were cases of Legg-Perthe disease with a wandering acetabulum, paralytic dislocations and congenital dislocations of the hip.

New Approach to the Knee Joint.—Mader [34] states that the patella is the chief obstacle in approaching the knee joint and that it has no important function, being a deterrent rather than an aid to movement. After studies on 20 cadavers had shown that extension of the knee was not disturbed by removal of the patella, he devised an operative approach as follows: a curved infrapatellar incision was made, and the skin flap was reflected upward. The tendon overlying the patella was split longitudinally, and the patella was dissected out subperiosteally. The joint was then exposed by lengthening the longitudinal incision in the quadriceps tendon. This method gave excellent exposure of the joint. Normal function has been observed in the extensor apparatus after the operation.

Amputation for Arteriosclerotic Gangrene.—Taylor [35] presents a series of 137 major amputations on 117 patients for arteriosclerotic gangrene with or without diabetes. He discusses the relation of the amputation stump to morbidity and mortality. There were 44 deaths, giving an amputation mortality of 32 per cent and a case mortality of 37.6 per cent. In cases of diabetes and arteriosclerotic gangrene the mortality was 34.4 and 52.5 per cent when local or systemic infection was an added complication. In cases in which diabetes was not present the mortality was 27.7 per cent. When "fascial layer closure" was carried out there was a mortality of 43.4 per cent, and nearly half of the deaths (46 per cent) were directly or indirectly due to an infected or a nonhealing stump. The mortality dropped to 19 per cent when

33. Nachlas, I. W.: South. M. J. **32**:565, 1939.
34. Mader, V. O.: Canad. M. A. J. **42**:17, 1940.
35. Taylor, F. W.: Arteriosclerotic Gangrene: Relation of Amputation Stump to Morbidity and Mortality, J. A. M. A. **113**:1196 (Sept. 23) 1939.

there was no closure and to 16 per cent when a loose skin closure alone was done. Taylor concludes that "anatomic fascial plane suture" of the stump should be reserved for the exceptional case in which there is no infection and an abundant blood supply is present.

Amputation for Advanced Peripheral Arterial Obliterative Disease.—This report by Faxon [36] is based on 204 single and 58 bilateral amputations. The conditions were subdivided into three clinical entities, Buerger's disease, peripheral arteriosclerosis and peripheral arteriosclerosis with diabetes. Guillotine or amputation preliminary open operation was carried out in 52 instances on critically ill patients as a life-saving measure. The midportion of the lower part of the leg was the site of choice. Secondary closed amputations at a higher level were carried out in 84 per cent of patients who survived the guillotine procedure. Ten per cent of the entire series of patients underwent the open preliminary procedure. Forty per cent of all the patients underwent closed amputations as a primary procedure. In only 5 instances were drains used. It is felt that avoidance of drains in amputation has been a great factor in reducing the mortality from progressive obliterative disease to 13.1 per cent. "Low thigh amputation" is considered the safest of major amputations. The Gritti-Stokes amputation is the most satisfactory for patients whose general condition precludes use of a prosthesis.

Transplantation of the Fibula to the Tibia.—Marconi [37] after reviewing the various methods which have been used for partial or complete transplantation of the fibula to the tibia reports 4 personally observed cases in which this operation was performed. His first patient was a boy aged 7 years with complete destruction of a portion of the tibia by osteomyelitis. A lateral transplantation was performed of the remaining (upper) end of the tibia to the fibula. Four years later walking was entirely normal. Two operations were necessary to secure union. The second patient was a boy aged 5 years. In his case also there was complete loss of the middle third of the tibia following removal of sequestrums. Transplantation of the fibula into the remaining ends of the tibia was done. Bony union followed the operation. The result eighteen months later showed 3 cm. shortening, with some limitation of motion at the ankle joint. There was no other deformity, and the child walked well. The third patient, 4 years old, had a loss of the lower part of the tibia following necrosis from diathermy. A portion of the fibula was implanted into the astragalus below and into

36. Faxon, H. H.: Major Amputations for Advanced Peripheral Arterial Obliterative Disease, J. A. M. A. **113**:1199 (Sept. 23) 1939.

37. Marconi, S.: Chir. d. org. di movimento **24**:552, 1939.

the tibia above. A second operation was required for fracture, with metallic fixation. Two years after the first treatment the patient was beginning to walk and there was solid union. The fourth patient, 16 years old, had lost almost the entire upper third of the tibia from osteomyelitis. An end to end transplant of the fibula was done. There was suppuration for a prolonged period. One year from the beginning of treatment the patient was beginning to walk. The author feels that various modifications of this method must be adopted to secure the best statics in the individual case.

Operation for Correction of Hammer Toe.—With the region under local block anesthesia, a hockey-stick cutaneous incision is made on the dorsum of the toe, somewhat lateral to the midline, without a tourniquet.[38] The flattened tendinous expansion of the extensors, which is intimately interwoven with the joint capsule, is exposed. A tongue-shaped flap with the base attached to the middle phalanx is exposed. A small dorsal bony prominence over the dorsum of the head of the proximal phalanx is sometimes shaved off. A subcutaneous plantar tenotomy and capsulotomy from one collateral ligament to the other are performed. It is important to obtain slight overcorrection of the plantar flexion contracture. The tongue-shaped flap is then resutured with reduplication to the proximal stump of the tendon and capsule by means of fine chromic mattress sutures. If dorsiflexion contracture is present at the metatarsophalangeal joint, it is released subcutaneously with a tenotomy knife in the thorough manner described. The toe is splinted with well fitted, loosely strapped whalebones. Immobilization should be thoroughly carried out for about three or four weeks after the operation. The patient may be permitted to walk a few days after the operation, wearing shoes cut over the toes. In cases in which plantar flexion contracture at the distal interphalangeal joint is also present, fusion is usually performed by shaving off the articular cartilage and performing the capsuloplasty described. In cases in which a painful corn is present at the tip of the toe, a U-shaped incision is made parallel to the distal edge of the nail and slightly to the plantar side. The distal part of the nail phalanx is removed. Seventeen cases (30 toes) are included in this report. Good results were obtained in 14 (26 toes), a fair result in 1 (1 toe) and poor results in 2 (3 toes). The author feels that by this technic the correction of the deformity is obtained with the least sacrifice of appearance and of function.

[ED. NOTE: While this operation may lead to the most nearly perfect cosmetic result, there are a number of simple but adequate procedures to relieve pain and permit function.]

38. Lapidus, P. W.: J. Bone & Joint Surg. **21**:977, 1939.

RESEARCH

Temperature-Controlled Healing of Experimental Fractures.—Speed and Fell [39] experimented with 66 guinea pigs, 45 of which lived to complete the experiments, to determine the effect of a raised temperature on the healing of fractures. "Both bones of the right foreleg of each animal in one group were fractured in the middle third. All the skin from the mid-upper right leg, down to and including the skin of the foreleg, of each animal in a second group was removed, and an amputation was performed at the wrist joint. The two bones of the foreleg were fractured in a manner similar to that of the first group, and the skinned fractured leg was then inserted into the abdominal cavity through a small aseptic incision made a little below the costal margin. The peritoneum and muscles of the abdominal wall and those of the midportion of the upper leg were sutured together." At the end of four weeks the animals were killed. Seventeen had survived. Of a control group of 10 guinea pigs, in which the bones of one foreleg were fractured and the leg was not buried within the abdomen, 5 tolerated splints from ten to twenty-one days and 5 were not splinted. The fracture area showed bony, fibrous and cartilaginous callus with a histologic picture similar to that observed in the control group. Although the differences in the two groups were not marked, it was felt that the legs which were buried in the abdomen and maintained at a higher temperature than those left outside exhibited a less bulky callus, a more matured bony callus and a much less fibrous and cartilaginous callus than did the unburied legs.

General Reactions of the Skeleton After Fracture.—Roche [40] attempts to show that there are general as well as local reactions which occur in the skeleton after fracture of a single bone. Phosphatase is an enzyme which hydrolyzes phosphoric esters into phosphate ions and produces a concentration of ions favorable to the local production of tricalcium phosphate. Phosphatase is abundant in the skeletal parts of young animals, which are undergoing rapid ossification. The bones of adult animals are nearly barren of phosphatase activity but can be reactivated by certain substances, such as the ionizable salts of magnesium. It has been shown that the callus and the neighboring region of a fracture are the site of increased phosphatase activity, and the author has sought to determine whether this is a purely local affair or whether the entire skeleton takes part in it. Fractures of the humerus in the pigeon were studied, and pseudarthroses of the femur in rats were investigated. The following conclusions were reached: 1. The

39. Speed, K., and Fell, E. H.: J. Bone & Joint Surg. **21**:1005, 1939.
40. Roche, J.: J. de chir. **53**:737, 1939.

callus of fractured bones presents, in general, phosphatase activity of the same order as that of the diaphysial and epiphysial regions of which it is a part. The important augmentation of the phosphatase activity comes a few days after the fracture, before any callus forms, and it disappears in fifteen or sixteen days. These phenomena indicate the putting into play of mechanisms unloosed by the fracture but independent of the evolution of the fracture. Whether the callus is ossified or whether it is converted into a pseudarthrosis, no difference is noted in the modification of enzyme activity in the bone fragments. 2. It was found that the intact bones of an animal with a fractured bone present an increase in phosphatase activity simultaneous with that observed in traumatized bone. The fact that this general reaction occurs early, before there is any possibility of repair, indicates the putting into effect of general mechanisms affecting the biochemistry of the skeleton, which are stimulated or unloosed by the lesion. The author has also made observations on general modifications of the composition of the skeleton after fracture of one bone. Numerous experiments by other authors have demonstrated a slow and progressive resorption of the bony tissue of fractured limbs, which is for the purpose of enrichment of the callus with salts by "local calcium mutation." The author has made the following observations as to general reactions accompanying this local reaction. 1. Modifications of composition appear simultaneously in all parts of the skeleton, being most marked in the immediate site of the lesion. They are characterized at first by demineralization of all the parts during a period of about twenty-five days, followed by a more or less complete repair of the losses previously undergone. This process is independent of the evolution of the callus, occurring even in pseudarthrosis. 2. The intact skeletal bone presents qualitively the same modifications as the fractured bone at different times in the experiment, though these modifications are less intense in the normal than in the fractured bone. The author concludes from these facts that the skeleton constitutes a physiologically homogeneous system the calcification of which is governed by general, not local, mechanisms.

Effect of Roentgen Rays on Bones.—Bade and Küntscher [41] studied the effect of roentgen rays on the bones of dogs after resection of a piece of the shaft. Marked changes were seen in the bone cells and in the bone marrow after six doses of 400 r each. After such treatment there was no compensatory thickening of the ulna, but fracture from weakening of the ulna was observed in four to six weeks. Histologic studies are not reported.

41. Bade, H., and Küntscher, G.: Fortschr. a. d. Geb. d. Röntgenstrahlen **60**: 235, 1940.

Effect of Experimentally Produced Tumors on the Skeletal System.—A study [42] was made to determine the effects of anthracene-produced tumors on skeletal tissue. The agent used was dibenzanthracene. Thirty-five rats were treated, and 16 had tumors ranging in size from that of a pea to that of an orange. Most of the tumors, even though they abutted on skeletal tissue, provoked little or no periostitis, and none showed bone formation. Histologically most of the tumors were cellular fibrosarcomas with elements of rhabdomyosarcoma and liposarcoma. There was no evidence of osteogenic tumor. Periosteal reaction was minimal even when the tumor lay against the outer lamellas of the cortex. In some cases, however, the tumor did invade the contiguous bone and joint to some extent. Intra-articular injection resulted in a sarcoma which invaded most of the structures of the knee joint and extended into the marrow cavity at the distal end of the femur. Implantation of dibenzanthracene into the marrow of the tibia did not produce an osteogenic tumor.

Motion in the Vertebral Column.—Elward [43] presents an extensive review of the literature on motions of the spine, followed by roentgen studies of the movements of the dorsolumbar and lumbosacral portions of the spine in a 16 year old girl. He concludes from his studies that the range of extension is greater than the range of flexion in the lumbar portion of the spine and that flexion at the hips accounts for the apparent greater range of flexion over extension. In this observation he confirms the work of Brailsford, who found extension to be greater than flexion in the lumbar part of the spine. The work of Wiles and others concerning the slight anterior and posterior displacement of vertebrae on adjacent vertebrae during flexion and extension was not confirmed in this study. The author concludes that the spinal column is not a single hinge but a multiplicity of interacting hinges, or, more precisely, limited universal joints, the nucleus pulposus acting somewhat in the manner of a ball bearing. There is no single center of motion except that of the mass motion centering in the hip joints.

42. Sutro, C. J., and Pomerantz, L.: Effect of Experimentally Found Tumors on Musculoskeletal System of Rats, Arch. Surg. **38**:1132 (June) 1939.

43. Elward, J. F.: Am. J. Roentgenol. **42**:81, 1939.